ACUTE KIDNEY INJURY IN THE MEDICAL WARDS OF G.R.H MADURAI – A PROSPECTIVE STUDY

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"ACUTE KIDNEY INJURY IN THE MEDICAL WARDS OF G.R.H MADURAI – A PROSPECTIVE STUDY"** submitted by **Dr. ARUN MATHAI MANI** to the Tamil Nadu Dr. M.G.R Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D DEGREE (Branch–I) GENERAL MEDICINE is a bonafide research work carried out by him under direct supervision & guidance.

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DECLARATION

I, **Dr. ARUN MATHAI MANI** solemnly declare that the dissertation titled **'ACUTE KIDNEY INJURY IN THE MEDICAL WARDS OF G.R.H MADURAI – A PROSPECTIVE STUDY'** is a bonafide work done by me.

I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree and diploma to any university, board either in India or abroad.

The dissertation is submitted to The Tamil Nadu Dr.M.G.R. Medical University, towards partial fulfilment of requirement for the award of M.D. Degree in GENERAL MEDICINE (BRANCH –I)

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INTRODUCTION

Acute kidney injury is the new consensus term for acute renal failure.[1]Acute kidney injury (AKI) is a syndrome that takes on different forms. The severity of this syndrome is also variable. It refers to a clinical syndrome characterised by a rapid (hours to days) decrease in renal excretory function, with the accumulation of products of nitrogen metabolism such as creatinine and urea and other clinically unmeasured waste products. Other common clinical and laboratory manifestations include decreased urine output (not always present), accumulation of metabolic acids, and increased potassium and phosphate concentrations.[2,3,4]

AKI is the most common renal emergency in India. Around 1.5% of patients that are admitted to hospitals are referred to nephrology units for acute kidney injury.[5,6,7] Worldwide incidence of AKI is variable,[8,9] and even more among the developed and the developing countries.[10] The incidence of AKI varies greatly. It depends on the setting in which kidney injury occurs.[11]

The data that is available regarding the overall epidemiology of AKI is very limited. However it is very important to know the

epidemiology and clinical features of AKI, so as to execute adequate means for tackling the problem and to boost preventive strategies.[12]

Statistics which are based on a referral to a renal replacement therapy unit suggest that the problem is more common in the tropics.[13]

Despite advances in renal replacement therapy, the mortality in AKI remained more or less same in the last five decades. Several factors redound to this persistently high mortality. They include reasons such as a more elderly population with AKI and the fact that patients with more severe ailments survive long enough to develop kidney injury.[14] Recent data have shown that even small changes in renal function are associated with a substantial increase in mortality.[14,15]

The etiological spectrum of AKI is notably different between developing and developed nations. It is related to environmental, social and economic circumstances. Sepsis, surgery and trauma are the most common causes of AKI in developed countries. In developing countries, acute diarrheal diseases and tropical diseases still prevail.[16] The aetiology, course, and outcome of AKI differ in various parts of India[5,6,17]

In 2004, the Acute Dialysis Quality Initiative (ADQI)[1,18-23] group, comprising experts in the fields of nephrology and critical care medicine, published the RIFLE classification. This was a new consensus and

evidence-based definition for AKI.[1] The RIFLE classification defines three grades of severity and two clinical outcomes of acute kidney injury. The three grades of severity (Risk, Injury and Failure) based on changes to serum creatinine and urine output. The two clinical outcomes are Loss and End-stage. In 2007, a modified version of the RIFLE criteria was published by the AKI Network (AKIN), an international collaboration of nephrologists and intensivists, known as the AKIN criteria.[24]

REVIEW OF LITERATURE

DEFINITION AND CLASSIFICATION

Acute kidney injury (AKI) is a protean syndrome of varied severity. It is characterized by a rapid (hours to weeks) decline in the glomerular filtration rate (GFR) and retention of nitrogenous waste products such as blood urea nitrogen (BUN) and creatinine.[2,3]In recent years, it was realised that the time-honoured term acute renal failure (ARF) does not sufficiently describe the dynamic process propagating across initiation, maintenance, and recovery phases. Each phase may be of changing duration and severity.

The proposed alternative term acute kidney injury has much to recommend it. It better captures the diverse nature of this syndrome. Hence it has entered into widespread clinical use.

Historically, patients with AKI have been classified as being non-oliguric (urine output >400 mL/day), oliguric (urinary out-put <400 mL/day), or anuric (urinary output <100 mL/day).[25] Lower levels of urinary output reflects a more severe initial injury. It has implications for volume overload and electrolyte disturbances. It also has prognostic

significance. However, therapeutic manipulation of the urine output does not change this bad prognostic association.

For purposes of diagnosis and management, AKI has been divided into three categories[26]

1. Diseases characterized by renal hypoperfusion in which the integrity of renal parenchymal tissue is preserved (prerenal AKI),
2. Diseases involving renal parenchymal tissue (intrinsic AKI),
3. Diseases associated with acute obstruction of the urinary tract (postrenal AKI).

Most cases of acute intrinsic AKI are caused by ischemia or nephrotoxins and are classically associated with ATN.

AKI may occur in with either a previously normal renal function or as an acute deterioration in function in the presence chronic kidney disease.

The etiology and outcome of AKI is heavily influenced by the circumstances in which it occurs. That is whether it develops in the community or in the hospital. It is also important to distinguish whether the kidney injury occurs as an isolated process, which is more common in community-acquired AKI, or if it occurs as part of multiorgan

dysfunction syndrome. In the former, management is initially, conservative and follows an expectant approach. Renal replacement therapy is deferred when possible while awaiting the spontaneous recovery of renal function. In critically ill patients with multiorgan failure, dialysis should be started earlier. The goal is such cases is not simply control of azotemia but rather of renal support in an attempt to stabilize and optimize the physiologic parameters.[27]

More than 35 different definitions of AKI have been used in the recent literature.[28] In 2007, the Acute Kidney Injury Network (AKIN), organized a summit of nephrology and critical care societies from around the world. The group endorsed the RIFLE criteria with a small modification to include small changes in serum creatinine ($\geq$ 0.3 mg/dl or $\geq$ 26.5 mmol/l) when they occur within a 48-hour period.[24] Two recent studies examining large databases in the USA[29] and Europe[30] validated these modified criteria. Thakar et al. found that increased severity of AKI was associated with an increased risk of death independent of comorbidity.[31]

DIAGNOSTIC CRITERIA FOR ACUTE KIDNEY INJURY[24]

An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours).

Classification/staging system for acute kidney injury[24]

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dl or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg per hour for more than 6 hours
2	Increase in serum creatinine to more than 200% to 300% (> 2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours
3	Increase in serum creatinine to more than 300% (> 3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dl with an acute increase of at least 0.5 mg/dl, individuals who receive RRT)	Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours

A big hurdle in the investigation and treatment of AKI is the timely identification of the syndrome. It is difficult to easily and reliably

measure rapid changes in the GFR. Although the severity in reduction in GFR correlates with the onset of oliguria, the latter is insensate marker of the syndrome. This is because many patients with severe renal failure will remain non-oliguric. In AKI, there is poor agreement between serum creatinine and GFR. This is true at least until a serum creatinine has reached a steady state. Even then, the absolute increase in serum creatinine must take into reckoning variability in creatinine production rates.[42]

As a result, definitions of AKI that are based on a fixed increment in serum creatinine would be expected to be biased toward making an early diagnosis in well-muscled as compared with malnourished subjects or in men as compared with women.

INCIDENCE

Acute kidney injury is a common and important diagnostic and therapeutic challenge for clinicians.[32]The incidence of AKI is difficult to estimate because no registry of its occurrence exists and because up until recently there was no standardized definition. From a variety of predominantly single centre studies it is estimated that 5% to 7% of hospitalized patients develop AKI.[33-36] More detailed information is available regarding its development in the intensive care unit (ICU)

environment, where approximately 25% to 30% of unselected patients develop some degree of AKI, although again estimates vary considerable depending on the definition used and the population case mix. Renal replacement therapy is typically required in 5% to 6% of the general ICU population or 8.8 to 13.4 cases per 100,000 population/year[37-42] AKI is also a major medical complication in the developing world and in the tropics.[33] In this setting, diarrheal illnesses, infectious diseases like malaria and leptospirosis, and natural disasters such as earthquakes are common.[33] AKI is associated with a greatly increased risk of in-hospital mortality. In those admitted in the intensive care units, mortality rates may exceed 50%.[33]

AKI IN THE DEVELOPING WORLD

The epidemiology of AKI differs greatly between developed and developing countries. This is due to the differences in geography, demographics, economics, and co morbid diseases. While certain features of AKI are common to both, many aetiologies for AKI are region-specific such as infectious causes such as malaria and leptospirosis, envenomations from snakes, spider and caterpillar bites, and bee stings; and crush injuries from earthquakes and resultant rhabdomyolysis.[44]Factors responsible for this higher incidence of AKI in

the tropics include hot climate in connection with excessive sweating, increased predisposition to hypovolemic insults, poor nutritional status and increased susceptibility to infections.

ETIOLOGY

The causes of AKI have traditionally been divided into three broad categories: prerenal azotemia, intrinsic renal parenchymal disease, and post renal obstruction.

Prerenal AKI
I.Hypovolemia
A. Increased extracellular fluid losses: hemorrhage
B. Gastrointestinal fluid loss: vomiting, diarrhea, enterocutaneous fistula
C. Renal fluid loss: diuretics, osmotic diuresis, hypoadrenalism, nephrogenic diabetes insipidus.
D. Extravascular sequestration: burns, pancreatitis, severe hypoalbuminemia
E. Decreased intake: dehydration, altered mental status
II. Altered renal hemodynamics resulting in hypoperfusion
A. Low cardiac output state: disease of the myocardium, valves, and pericardium (including tamponade); pulmonary hypertension or massive pulmonary embolism leading to right and left heart failure; impaired venous return (e.g., abdominal compartment syndrome or positive pressure ventilation)

B. Systemic vasodilatation: sepsis, antihypertensives, afterload reducers, anaphylaxis.
C. Renal vasoconstriction: hypercalcemia, catecolamines, calcineurin inhibitors, amphotericin B.
D. Impairment of renal autoregulatory responses: cyclooxygenase inhibitors (e.g., non-steroidal anti – inflammatory drugs), angiotensin – converting enzyme inhibitors, or angiotensin II receptor blockers.
E. Hepatorenal syndrome
Intrinsic AKI
I. Renovascular obstruction (bilateral, or unilateral in the setting of one kidney)
A. Renal artery obstruction: atherosclerotic plaque, thrombosis, embolism, dissection aneurysm, large vessel vasculitis
B. Renal vein obstruction : thrombosis or compression
II. Disease of the glomeruli or vasculature
A. Glomerulonephritis or vasculitis
B. Other : thrombotic microangiopathy, malignant hypertension, collagen vascular diseases (systemic lupus erythematosus, scleroderma), disseminated intravascular coagulation, preeclampsia
III. Acute tubular necrosis
A. Ischemia: causes are the same as for prerenal AKI, but generally the insult is more severe and / or more prolonged.
B. Infection, with or without sepsis syndrome
C. Toxins:

1. Exogenous: radiocontrast, calcineurin inhibitors, antibiotics (e.g., aminoglycosides), chemotherapy (e.g., cisplatin), antifungals (e.g., amphotericin B), ethylene glycol, snake bites.
2. Endogenous : rhabdomyolysis, haemolysis
IV. Interstitial nephritis
A. Allergic: antibiotics (β – lactams, sulfonamides, quinolones, rifampicin), nonsteroidal anti – inflammatory drugs, diuretics, other drugs.
B. Infection: pyelonephritis (if bilateral)
C. Infiltration: lymphoma, leukemia, sarcoidosis
D. Inflammatory, nonvascular : Sjogeren's syndrome, tubulointerstitial nephritis with uveitis
V. Intratubular obstruction
A. Endogenous : myeloma proteins, uric acid, tumor lysis syndrome
B. Exogenous: acyclovir, gancyclovir, methotrexate, indinavir
Postrenal AKI (Obstruction)
I.Ureteric (bilateral, or unilateral in the case of one kidney): calculi, blood clots, sloughed papillae, cancer, external compression (e.g., retroperitoneal fibrosis)
II. Bladder neck: neurogenic bladder, prostatic hypertrophy, calculi, blood clots, cancer.
III. Urethra : stricture or congenital valves

PRERENAL AZOTEMIA (PRERENAL AKI)

Prerenal AKI is the most common cause of AKI and is an appropriate physiologic response to renal hypoperfusion.[2,12,43] By definition, the integrity of renal parenchymal tissue is maintained and GFR is corrected rapidly with restoration of renal perfusion. Severe renal hypoperfusion may cause ischemic AKI. Thus, prerenal AKI and ischemic AKI are manifestations of the same spectrum of renal hypoperfusion. The clinical and biochemical features of prerenal AKI and ischemic AKI may coexist in many patients.

Prerenal AKI can complicate any disease characterized by hypovolemia, low cardiac output, systemic vasodilatation, or intrarenal vasoconstriction. Hypovolemia leads to a fall in mean systemic arterial pressure. This in turn, activates carotid sinus and cardiac baroreceptors. This initiates a series of neural and humoral responses. This includes activation of the sympathetic nervous system, renin-angiotensin-aldosterone system and release of antidiuretic hormone.[44-46] Nor epinephrine, angiotensin II, and antidiuretic hormone act in synchrony. They do so to maintain BP, cardiac and cerebral perfusion. They inhibit salt loss through sweat glands, by stimulating vasoconstriction in musculocutaneous and splanchnic circulations, by stimulating thirst and

salt appetite, and by promoting renal salt and water retention. Glomerular perfusion, filtration rate and ultra filtration pressure are preserved during mild hypoperfusion through compensatory mechanisms. Stretch receptors present in the walls of afferent arterioles detect a reduction in perfusion pressure. This triggers relaxation of the afferent arteriolar smooth muscle cells and vasodilatation. Intrarenal biosynthesis of vasodilator prostaglandins (e.g., prostacyclin, prostaglandin E_2), kallikrein and kinins, and possibly nitric oxide (NO) is enhanced. Angiotensin II may induce preferential constriction of efferent arterioles, probably because most angiotensin II receptors are found at this location.[47] As a result, intraglomerular pressure is preserved, the fraction of renal plasma that is filtered by glomeruli (filtration fraction) is increased, and GFR is maintained. These compensatory renal responses are overwhelmed during states of moderate to severe hypoperfusion, and AKI ensues. Auto regulatory dilatation of afferent arterioles is maximal at a mean systemic arterial blood pressure of about 70 to 80 mm Hg, and hypotension below this level is associated with a precipitous decline in glomerular ultrafiltration pressure and GFR.[48,49]

Several classes of commonly used drugs impair renal adaptive responses and can convert compensated renal hypoperfusion to overt

prerenal AKI or trigger progression of prerenal AKI to ischemic AKI.[50] Non-steroidal anti-inflammatory drugs (NSAIDs), including cyclooxygenase II (COX-II) inhibitors, inhibit renal prostaglandin biosynthesis. They do not compromise GFR in normal individuals but may precipitate prerenal AKI in subjects with true hypovolemia or decreased effective arterial blood volume, or in patients with CKD in whom GFR is maintained in part by prostaglandin-mediated hyperfiltration through remnant nephrons.[51-54] Similarly, inhibitors of angiotensin-converting enzyme (ACE) and angiotensin II receptor blockers (ARBs) may trigger prerenal AKI in individuals in whom intraglomerular pressure and GFR are dependent on angiotensin II. This is seen in bilateral renal artery stenosis or unilateral stenosis in a solitary functioning kidney.[55] Here, angiotensin II preserves glomerular filtration pressure distal to renal arterial stenosis by increasing systemic arterial pressure and by triggering selective constriction of efferent arterioles. ACE inhibitors and ARBs blunt these compensatory responses and precipitate reversible AKI in such patients. ACE inhibitors or ARBs, like NSAIDs, may also precipitate prerenal AKI in patients with compensated renal hypoperfusion of other causes. This mandating close monitoring of the serum creatinine level when these drugs are given to patients with high-risk factors.

INTRINSIC AKI

The most common causes of intrinsic AKI are sepsis, ischemia, and nephrotoxins, both endogenous and exogenous. Ischemic ATN and toxic ATN account for about 80% to 90% of intrinsic AKI.[56,57] From a clinicopathologic viewpoint, it is helpful to categorize the causes of intrinsic AKI into the following categories:[26]

- Diseases involving large renal vessels,
- Diseases of the renal microvasculature and glomeruli,
- Ischemic and nephrotoxic ATN, and
- Other acute processes involving the tubulointerstitium.

DISEASES OF LARGE RENAL VESSELS, MICROVASCULATURE AND TUBULOINTERSTITIUM

Occlusion of large renal vessels is an uncommon cause of AKI. To affect BUN and serum creatinine, occlusion must be either bilateral or unilateral in patients with underlying chronic renal insufficiency or a solitary functioning kidney. Atheroemboli are the most common culprits and are usually dislodged from an atheromatous aorta during arteriography, angioplasty, or aortic surgery. Cholesterol emboli lodge in

medium or small renal arteries. Renal artery thrombosis is usually superimposed on an atheromatous plaque but may also complicate traumatic intimal tears or the site of surgical anastomosis after renal transplantation. Outside of the immediate post-transplantation period, renal vein thrombosis is an exceedingly rare cause of AKI and is usually encountered as a complication of the nephrotic syndrome in adults or of severe dehydration in children.

Virtually all diseases that compromise blood flow within the renal microvasculature may induce AKI. These include inflammatory (e.g., glomerulonephritis or vasculitis) and noninflammatory (e.g., malignant hypertension) diseases of the vessel wall, thrombotic microangiopathies, and hyperviscosity syndromes.

SEPSIS-ASSOCIATED AKI

Sepsis is an important cause of AKI in the developing world. It markedly accentuates the risk of mortality. Most cases of severe AKI typically occur in the setting of hemodynamic collapse. Sepsis induces renal hypoperfusion by provoking a combination of systemic vasodilatation and intrarenal vasoconstriction.[58-63]There is clear evidence of tubular injury in sepsis associated AKI. Post-mortem examinations of kidneys from individuals with severe sepsis also suggest that other factors

are involved. These factors which are related to inflammation and interstitial edema, must also be considered in the pathophysiology of sepsis-induced AKI.

ISCHEMIA-ASSOCIATED AKI

Even though healthy kidneys constitute only 0.5% of the human body, they receive 20% of the cardiac output and account for 10% of resting oxygen consumption. The renal medulla is also the site of one of the most hypoxic regions in the body. It is particularly vulnerable to ischemic damage. This is because of the architecture of the blood vessels that supply oxygen and nutrients to the tubules. Ischemia alone in a normal kidney is usually not sufficient to cause severe AKI. This fact is evidenced by the relatively low risk of severe AKI even after total interruption of renal blood flow during suprarenal aortic clamping or cardiac arrest. Clinically, AKI more commonly develops when ischemia occurs in the context of limited renal reserve. This can happen in chronic kidney disease or older age. It can also occur with coexisting insults such as sepsis, vasoactive or nephrotoxic drugs, rhabdomyolysis, and inflammatory states associated with burns and pancreatitis. Prerenal azotemia and ischemia-associated AKI represent a continuum of the manifestations of renal hypoperfusion. Prerenal AKI differs from

ischemic AKI. Ischemic AKI is associated with injury to renal parenchyma. This injury does not resolve immediately on restoration of perfusion. In its more extreme form, it may result in bilateral acute renal cortical necrosis and irreversible renal failure. Persistent preglomerular vasoconstriction is also an underlying cause of the reduction in GFR seen in AKI. Factors implicated for vasoconstriction are activation of tubuloglomerular feedback from enhanced delivery of solute to the macula densa following proximal tubule injury, increased basal vascular tone and reactivity to vasoconstrictive agents, and decreased vasodilator responsiveness. Back leak of filtrate across ischemic and denuded tubular epithelium and mechanical obstruction of tubules from necrotic debris also contributes to low GFR.

AKI IN DIARRHEAL DISEASE

Two major causes responsible for the wide prevalence of AKI in tropics are poor socioeconomic conditions and lack of clean water supply. Diarrheal diseases account for 5-10 million deaths/year. Diarrheal diseases are responsible for most cases of AKI in children in India. The incidence of ADD increases with the starting of summer. The maximum number of cases occurs during the rainy season. Early use of oral

rehydration therapy and an improvement in the standards of living in a decline of AKI related to diarrheal diseases.

Renal failure occurring in diarrheal disease is usually oliguric. Patients have metabolic acidosis out of proportion to the degree of renal failure. This is due to loss of bicarbonate in the diarrheal fluid. due to the loss of large amounts of potassium in the diarrheal stools, hypokalemia may occur. This can in turn cause paralytic ileus. Acute tubular necrosis is the most common histological lesion seen in renal failure associated with diarrheal disease. Acute cortical necrosis can also occur.

NEPHROTOXIN-ASSOCIATED AKI

The kidney has very high susceptibility to nephrotoxicity due to extremely high blood perfusion and concentration of circulating substances along the nephron where water is reabsorbed and in the medullary interstitium; this results in high-concentration exposure of toxins to tubular, interstitial, and endothelial cells. All structures of the kidney are vulnerable to toxic injury, including the tubules, interstitium, vasculature, and collecting system. As with other forms of AKI, risk factors for nephrotoxicity include older age, chronic kidney disease (CKD), and prerenal azotemia. Hypoalbuminemia may increase the risk of some forms of nephrotoxin-associated AKI due to increased free

circulating drug concentrations. Nephrotoxic ATN complicates the use of many structurally different drugs and poisons.[64-68] In general, nephrotoxins cause renal injury by inducing a varying combination of intrarenal vasoconstriction, direct tubule toxicity, and intratubular obstruction.. The nephrotoxic potential of most agents is dramatically increased in the presence of borderline or overt renal ischemia, sepsis, or other renal insults.

CONTRAST AGENTS

Iodinated contrast agents used for cardiovascular and CT imaging are a leading cause of AKI. Acute intra-renal vasoconstriction is an important pathophysiologic event in AKI associated with radiocontrast agents (contrast nephropathy). Contrast nephropathy typically presents as an acute decline in GFR within 24 to 48 hours of administration, a peak in serum creatinine value after 3 to 5 days, and return of the serum creatinine value to the "normal" range within 1 week.[106,107] Individuals with chronic renal insufficiency (serum creatinine >2.0 mg/dL) are at the greatest risk of contrast-induced renal injury.[69] Other risk factors include diabetic nephropathy, congestive heart failure, jaundice, volume depletion, multiple myeloma, the volume of contrast used, and the coincident use of ACE inhibitors or NSAIDs. Patients usually present

with benign urine sediment, concentrated urine, and low fractional excretion of Na^+ and, thus, have many features of prerenal AKI; however, in more severe cases, tubule cell injury may be evident.

ANTIBIOTICS

Therapeutic agents that are directly toxic to renal tubule epithelium include antimicrobials such as aminoglycosides, amphotericin B, acyclovir, indinavir, cidofovir, pentamidine, and foscarnet.[70-73]

Nonoliguric AKI (i.e., without a significant reduction in urine volume) accompanies 10–30% of courses of aminoglycoside antibiotics, even when plasma levels are in the therapeutic range. Aminoglycosides are polycations and are freely filtered across the glomerular filtration barrier and accumulated by proximal tubule cells by absorptive endocytosis after interaction with negatively charged phospholipid residues on brush border membranes. Important risk factors for aminoglycoside nephrotoxicity include use of high or repeated doses or prolonged therapy, pre-existing renal insufficiency, advanced age, volume depletion, and the coexistence of renal ischemia or other nephrotoxins.[74] Although the precise sub cellular mechanisms by which aminoglycosides perturb renal function has not yet been fully elucidated, gentamicin has been demonstrated to bind to megalin, an endocytic

receptor in the clathrin-coated pits of the apical cell membrane. When endocytosed, this complex may induce cellular injury by inhibiting endosomal fusion events. AKI typically manifests after 5–7 days of therapy and can present even after the drug has been discontinued. Hypomagnesaemia is a common finding and suggests coexistent injury to the thick ascending limb of the loop of Henle, the major site of Mg^{2+} reabsorption.

Nephrotoxicity from amphotericin B is dose and duration dependent. AKI is almost invariable in patients receiving cumulative doses of amphotericin B of more than 1 g and is a common complication even with lower doses.[75] This drug binds to tubular membrane cholesterol and introduces pores. Amphotericin B induces direct renal vasoconstriction and exerts direct toxicity on a variety of tubular segments. The tubular dysfunction is manifested by an increase in tubuloglomerular feedback with resultant suppression of GFR, ATN, hypomagnesaemia, hypophosphatemia, hypocalcaemia, and a renal tubular acidosis due to back leakage of secreted H^+ in the distal cortical nephron. ATN due to amphotericin B is typically reversible, but chronic use can lead to nephrocalcinosis. Clinical features of amphotericin B

nephrotoxicity include polyuria, hypomagnesaemia, hypocalcaemia, and non-gap metabolic acidosis.

High-dose intravenous acyclovir causes AKI within 24 to 48 hours in 10% to 30% of patients, particularly if they are volume depleted or if the drug is administered as a bolus.[76] AKI is usually nonoliguric; frequently associated with colic, nausea, and vomiting; and appears to be induced by intratubular precipitation of acyclovir crystals. A similar syndrome in now recognized in patients receiving the oral antiretroviral drug indinavir.[77] Asymptomatic crystaluria in seen in up to 10% of patients, with half this number presenting with loin pain and hematuria.

A Fanconi-like syndrome is seen in up to 40% of patients receiving adefovir, a nucleoside reverse transcriptase inhibitor due to a direct toxic effect on tubular cell mitochondrial function. A similar syndrome has also been described with tenofovir. Cidofovir, a nucleotide analog used to treat cytomegalovirus infections is also nephrotoxic. Pentamidine induces AKI in 25% to 95% of patients, usually during the second week of therapy and frequently in association with hypomagnesaemia, hypo- or hyperkalemia, and a distal renal tubular acidosis.

The mechanism of injury is unclear but may involve an immune process, because AKI does not appear to be dose dependent and is often

associated with pyuria, hematuria, proteinuria, and casts. Foscarnet causes a distinct pattern of renal injury characterized by nonoliguric, often polyuric, AKI within 7 days, hyperphosphatemia, ATN, interstitial fibrosis, and a slow recovery that may take months. ATN complicates up to 70% of courses of cisplatin and ifosfamide, two commonly used chemotherapeutic agents.

Vancomycin may be associated with AKI, particularly when trough levels are high, but a causal relationship with AKI has not been definitively established.

Foscarnet, pentamidine, and cidofovir (less commonly prescribed antimicrobials) are also frequently associated with AKI due to tubular toxicity.

TOXIC INGESTIONS

Poisoning with Super Vasmol; a commonly used hair dye, in South India have been reported.[78-80] This dye is composed of paraphenylenediamine (PPD), ethylene diamine tetra acetic acid (EDTA), propylene glycol, liquid paraffin, cetostearyl alcohol, sodium laurylsulphate and resorcinol. Resorcinol, being a phenol, has been postulated to cause renal failure, while EDTA which may be present may cause hypocalcaemia. The most common cause of death in these patients

is acute renal failure, which occurs as a result of the nephrotoxic components of this hair dye, as well as due to rhabdomyolysis. Myoglobin, which was released as a result of rhabdomyolysis, has been implicated in heme induced renal damage, mainly by causing oxidative damage to the renal tubules. However, renal failure can also occur as a result of other nephrotoxic chemicals which are present in the Super Vasmol dye. Apart from PPD, propylene glycol and resorcinol which are present in the Super Vasmol dye can result in acute tubular necrosis.

The extensive use of copper sulphate in leather industry, its low cost and easy availability are the main reasons for its use as a mode of suicide among the poor socioeconomic groups in India. AKI develops in 20-40% of patients with acute copper sulphate poisoning and is invariably oliguric.[81,82] The possible mechanisms of kidney damage include; pre-renal failure due to dehydration (vomiting, diarrhoea, reduced fluid intake), haemoglobinuria, sepsis, rhabdomyolysis, direct copper toxicity on proximal tubules and secondary effects of multi organ dysfunction. The recovery of renal function following copper sulphate ingestion is observed to be slow and incomplete.

Ethylene glycol, present in automobile antifreeze, is metabolized to oxalic acid, glycolaldehyde, and glyoxylate, which may cause AKI

through direct tubular injury. Diethylene glycol is an industrial agent that has been the cause of outbreaks of severe AKI around the world due to adulteration of pharmaceutical preparations. The metabolite 2-hydroxyethoxyacetic acid (HEAA) is thought to be responsible for tubular injury. Melamine contamination of foodstuffs has led to nephrolithiasis and AKI, either through intratubular obstruction or possibly direct tubular toxicity. Aristolochic acid was found to be the cause of "Chinese herb nephropathy" and "Balkan nephropathy" due to contamination of medicinal herbs or farming. The list of environmental toxins is likely to grow and contribute to a better understanding of previously catalogued "idiopathic" chronic tubular interstitial disease, a common diagnosis in both the developed and developing world.

SNAKE BITES AND AKI

Although nearly all snakes with medical relevance can induce AKI, it is unusual except with bites by *Russell's viper, E.Carinatus*, and members of the genera Crotalus and Bothrops. The most prevalent areas for these snakes are Asia and South America. In India AKI is mostly associated with *Russell's viper* and *E.carinatus* bites. In India, the incidence of AKI following snake bite is 13-32%[83]

The AKI following snake bite may be due to a number of factors like bleeding, hypotension, circulatory collapse, intravascular hemolysis, DIC, microangiopathic haemolytic anemia and direct nephrotoxicity of the venom. Renal histology shows predominantly either acute tubular or cortical necrosis. Early administration of ASV is vital in patients with evidence of systemic envenomation as it may prevent hematologic abnormalities and renal complications.

ENDOGENOUS TOXINS

Myoglobin, hemoglobin, uric acid, and myeloma light chains are the endogenous toxins that are most commonly associated with AKI.

PIGMENT INDUCED AKI

Renal dysfunction complicates approximately 30% of cases of rhabdomyolysis.[83-87] Rhabdomyolysis may result from traumatic crush injuries, muscle ischemia during vascular or orthopaedic surgery, compression during coma or immobilization, prolonged seizure activity, excessive exercise, heat stroke or malignant hyperthermia, infections, metabolic disorders (e.g., hypophosphatemia, severe hypothyroidism), and myopathies (drug-induced, metabolic, or inflammatory). In the tropics, common causes of non traumatic rhabdomyolysis producing myoglobinuric AKI are eclampsia, prolonged labour, poisoning with

mercuric chloride or zinc phosphide, status epilepticus, viral myositis, burns and electrical injury.[88]

Hemoglobin-induced ATN is rare and is most commonly encountered after blood transfusion reactions.[89] Acute hemolysis in G6PD deficient individuals is a frequent cause of AKI in some populations of our country, producing AKI in 5- 10% of cases.[6] Pathogenic factors for AKI include intrarenal vasoconstriction, direct proximal tubular toxicity, and mechanical obstruction of the distal nephron lumen when myoglobin or hemoglobin precipitates with Tamm-Horsfall protein (uromodulin, the most common protein in urine and produced in the thick ascending limb of the loop of Henle), a process favoured by acidic urine.[90-93]

Acute uric acid nephropathy typically complicates treatment of lymphoproliferative or myeloproliferative disorders and is usually associated with other biochemical evidence of tumor lysis such as hyperkalemia, hyperphosphatemia, and hypocalcemia.[94] Acute uric acid nephropathy is rare when plasma concentrations are less than 15 to 20 mg/dL but may be precipitated at relatively low levels by volume depletion or low urine pH. Casts, composed of filtered immunoglobulin light chains and other urinary proteins such as Tamm-Horsfall protein

(THP), induce AKI in patients with multiple myeloma (myeloma-cast nephropathy).[95]

AKI IN LEPTOSPIROSIS

In tropical countries, where the disease is endemic, leptospirosis is an important cause of AKI. The incidence of AKI varies from 10% to 60%, depending on the severity of the disease, age, and definition of AKI.[96] Renal involvement in leptospirosis can vary from a subclinical course, with mild proteinuria and urinary sediment abnormalities, to severe AKI. Acute kidney injury usually presents with a rapid elevation in serum urea and creatinine, and can be associated with jaundice. Kidney injury in patients with hyperbilirubinemia represents a severe form, frequently accompanied by oliguria-anuria.[97] Acute kidney injury due to leptospirosis usually presents in the non-oliguric form with hypokalemia, which can be detected in 41% to 45% of the patients with leptospirosis associated with AKI. Tubular dysfunctions, mainly of the proximal tubule, are very common, even in the absence of AKI. Alterations, such as bicarbonaturia, glycosuria, and a reduction in sodium proximal reabsorption and uric acid and phosphate excretion, have been observed, and a deficit in the urinary concentration can persist for prolonged periods.[98] Hypokalemia is a frequent finding in AKI of leptospirosis, and

can be observed in 45% to 74% of patients on hospital admission, requiring intravenous potassium replacement in 80% of the cases. In the AKI of leptospirosis, even oliguric patients do not usually have hyperkalemia. Hypokalemia is the most characteristic laboratory finding of AKI of leptospirosis. Thus, AKI of leptospirosis, regardless of its severity, hypercatabolism, rhabdomyolysis, acidosis, and oliguria, is characterized by normo- or hypokalemia. That is a relevant characteristic of AKI due to leptospirosis at the time of diagnosis. Another early characteristic of kidney injury is the ultrasound finding of enlarged kidneys, with relatively normal parenchymal echogenicity, indicating tubulointerstitial nephritis.[99] The major factors involved in the pathogenesis of AKI in leptospirosis are the direct nephrotoxic action of the leptospira and the toxin-induced immune response. Hemodynamic alteration, jaundice, and rhabdomyolysis are also associated with the genesis of AKI in leptospirosis. AIN is the major causing mechanism of AKI.[100]

PATHOPHYSIOLOGY OF KIDNEY DYSFUNCTION IN ACUTE KIDNEY INJURY

The effect of renal injury, whether from ischemia or from other causes, is a profound decrease in the GFR. This large decrease in filtration capacity of the kidney often occurs in the absence overwhelmingly evident damage to the kidney as seen on light microscopy. There are at least three major classic proposed mechanisms for the fall in GFR, as determined by micropuncture studies on animals and indirect methods in humans. The first mechanism is a drop in the filtration pressure in the glomerulus. This drop in pressure is caused by afferent arteriolar vasoconstriction and proximal tubular obstruction.[101] This first mechanism leads to a direct fall in the GFR. Afferent arteriolar vasoconstriction is thought to be a result of endothelial cell injury.[102] This leads to an imbalance in vasoactive substances, with a predominance of vasoconstrictive activity. The second mechanism, tubular back-leakage, leads to a fall in the effective GFR. Back-leakage of glomerular filtrate occurs in the setting of damage and loss of epithelial cells and loss of tight junctions between those cells that are critical to maintaining separation of tubular filtrate and the surrounding interstitium.[103] Tight junctions are disrupted in the setting of adenosine triphosphate (ATP)

depletion, allowing back-leakage of sodium and other solutes into the renal interstitium.[104]The third mechanism, tubular obstruction, is a result of cast formation from sloughed tubular epithelial cells as well as THP. THP tends to polymerize and form a gel that can further trap cells and tubular cell debris following AKI. The concentration of various molecules in the renal tubules in evolving ATN further promotes THP gel formation. Besides a fall in GFR, there is also a decreased ability of the kidney to concentrate urine following AKI. This is due in part to the loss of aquaporin water channel expression in different parts of the nephron including the collecting duct and the proximal tubules. Sodium and acid-base transporters are also dysregulated by kidney injury.

DISTANT ORGAN PATHOPHYSIOLOGY

AKI is a systemic disease, and with the availability of dialysis, most deaths during AKI are due to hypotension, cardiorespiratory failure, sepsis, and gastrointestinal bleeding. Organ cross-talk during AKI is being increasingly studied, and may help explain the excess morbidity and mortality associated with even mild degrees of acute kidney impairment. There is a strong association between AKI and acute lung injury, and the mortality rate during AKI rises from 50% to 80% when both lung and kidney are involved. Evidence for direct AKI-induced

distant organ dysfunction was demonstrated when clamping of the renal artery in rats increased pulmonary vascular permeability with microvascular inflammation and both leukocyte and RBC sludging. Acute ischemic kidney injury can also produce cross-talk between the kidney and bone marrow, perhaps supporting or enhancing the inflammation that is seen during AKI. Cross-talk between the kidney and liver has also been demonstrated in the setting of AKI. The injured kidney produces IL-6, which exerts local proinflammatory and distant anti-inflammatory effects.

COURSE OF ACUTE TUBULE NECROSIS

The clinical course of ATN can be divided into three phases: the initiation, maintenance phase, and recovery phases. The initiation phase is the period when patients are exposed to the ischemia or toxins and parenchymal renal injury is evolving but not yet established. ATN is potentially preventable during this period, which may last hours to days. The initiation phase is followed by a maintenance phase, during which parenchymal injury is established and GFR stabilizes at a value of 5 to 10 mL/min.[105-107] Urine output is usually lowest during this period. The maintenance phase typically lasts 1 to 2 weeks but may be prolonged for 1 to 11 months before recovery. The recovery phase is the period, during

which patients recover renal function through repair and regeneration of renal tissue. Its onset is typically heralded by a gradual increase in urine output and a fall in serum creatinine, although the latter may lag behind the onset of diuresis by several days. This post-ATN diuresis may reflect appropriate excretion of salt and water accumulated during the maintenance phase, osmotic diuresis induced by filtered urea and other retained solutes, and the actions of diuretics administered to hasten salt and water excretion.[108-110] Occasionally, diuresis may be inappropriate and excessive if recovery of tubule reabsorptive processes lags behind glomerular filtration, although this phenomenon is more common after relief of urinary tract obstruction.

DIAGNOSTIC EVALUATION

A graph of remote and recent serum creatinine levels versus time, incorporating drug therapy and interventions, is invaluable for differentiation of acute and chronic renal failure and the identification of the cause of AKI. When previous measurements are not available, anemia, hyperparathyroidism, neuropathy, band keratopathy, and radiologic evidence of renal osteodystrophy or small scarred kidneys are useful indicators of a chronic process. However, it should be noted that anemia may also complicate AKI, particularly if prolonged, and renal

size can be normal or increased in a variety of chronic renal diseases (e.g., diabetic nephropathy, amyloid, polycystic kidney disease). Once a diagnosis of AKI is established, attention should focus on the differentiation between prerenal, intrinsic renal, and postrenal AKI, and the identification of the specific causative disease.

Clinical Approach to the Diagnosis of Acute Kidney Injury

History, physical examination (including fundoscopy and weight), detailed view of hospital chart, previous records, and drug history
Urinalysis including specific gravity, dipstick, sulfosalicylis acid, microscopy, and staining for eosinophils
Flow chart of serial blood pressure, weight, BUN, serum creatinine, major clinical events, interventions, and therapies
Routine blood chemistry assays (BUN, creatinine, Na^{+},K^{+},Ca_2^{+},HCO_3^{-}, Cl^{-}, PO_4^{3-} and hematologic tests.
Selected special investigation: Urine chemistry, eosinophils, and/or immunoelectrophoresis Serologic tests: antiglomerular basement membrane antibodies, antineutrophil cytoplasmic antibodies, complement, antinuclear antibodies, serum protein electrophoresis, anti – streptolysin O or anti – DNAase titers

Radiologic evaluation : plain abdominal film, renal ultrasonography, intravenous pyelography, renal angiography, magnetic resonance angiography.
Renal biopsy

CLINICAL ASSESSMENT

Prerenal AKI should be suspected when the serum creatinine value rises after hemorrhage. Supportive findings on clinical assessment include symptoms of thirst or orthostatic dizziness and objective evidence of orthostatic hypotension (postural fall in diastolic pressure greater than 10 mm Hg) and tachycardia (postural increase of more than 10 beats/min). However, florid symptoms or signs of hypovolemia are usually not manifest until extracellular fluid volume has fallen by 10% to 20%. Nursing and pharmacy records should be reviewed for recent use of analgesics and anti-hypertensives. Consideration should be given to the misuse of illicit drugs such as cocaine. Clinical examination may show signs of chronic liver disease (e.g., palmar erythema, jaundice, telangiectasia, caput medusae, splenomegaly, ascites), advanced cardiac failure (e.g., peripheral edema, hepatic congestion, ascites, elevated jugular venous pressure, bibasilar lung crackles, pleural effusion,

cardiomegaly, gallop rhythm, cold extremities), or other causes of reduced effective critical blood volume.

Definitive diagnosis of prerenal AKI hinges on prompt resolution of AKI after restoration of renal perfusion. There is a high likelihood of ischemic ATN if AKI follows a period of severe renal hypoperfusion and persists despite restoration of renal perfusion. It should be noted, however, that significant hypotension is recorded in the case notes of less than 50% of patients with postsurgical ATN. The diagnosis of nephrotoxic ATN requires scouring of clinical, pharmacy, nursing, and radiology records for evidence of recent administration of nephrotoxic medications or radiocontrast agents. AKI after cancer chemotherapy suggests a diagnosis of tumor lysis syndrome and acute urate nephropathy, although other diagnoses must be considered. Pigment-induced ATN may be suspected if the clinical assessment reveals clues to rhabdomyolysis (e.g., seizures, excessive exercise, alcohol or drug abuse, muscle tenderness, limb ischemia) or hemolysis (e.g., recent transfusion).

Although most AKI is either prerenal or due to ischemic and nephrotoxic ATN, patients should be assessed carefully for evidence of other renal parenchymal diseases, because many of the latter are treatable and their diagnosis alters management and prognosis.

Increased urinary protein excretion, characteristically less than 1 g/d, is a common finding in ischemic or nephrotoxic AKI and reflects both failure of injured proximal tubule cells to reabsorb normally filtered protein and excretion of cellular debris (tubule proteinuria). Heavy proteinuria is also a frequent finding (80%) in patients with allergic interstitial nephritis triggered by NSAIDs. These patients have a glomerular lesion that is almost identical to minimal-change glomerulonephritis, in addition to acute interstitial inflammation. A similar syndrome has been reported in patients receiving other agents such as ampicillin, rifampicin, and interferon alfa. Hemoglobinuria or myoglobinuria should be suspected if urine is strongly positive for hemoglobin by dipstick but contains few RBCs and if the supernatant of centrifuged urine is pink and also positive for free hemoglobin. Hemolysis and rhabdomyolysis can usually be differentiated by inspection of plasma. The latter is usually pink in hemolysis, but not in rhabdomyolysis, because free hemoglobin (65,000 daltons) is a larger molecule than myoglobin (17,000 daltons) that is heavily protein bound and filtered slowly by the kidney.

CONFIRMATORY TESTS

The pattern of change in serum creatinine value often provides clues to the cause of AKI. Prerenal AKI is typified by rapid fluctuations

in creatinine that parallel changes in hemodynamic function and renal perfusion.

Imaging of the urinary tract by plain film of the abdomen, ultrasonography, computed tomography (CT), or magnetic resonance is recommended for most patients with AKI to distinguish between acute and chronic renal failure and exclude acute obstructive uropathy. The plain film of the abdomen, with tomography if necessary, usually provides a reliable index of kidney size and may detect Ca^{2+}-containing kidney stones. However, the capacity of ultrasonography to determine cortical thickness, differences in cortical and medullary density, and the integrity of the collecting system, in addition to kidney size, makes it the screening modality of choice in most cases of AKI. Although pelvicalyceal dilatation is usual in cases of urinary tract obstruction (98% sensitivity), dilatation may not be observed in the volume-depleted patient during the initial 1 to 3 days after obstruction when the collecting system is relatively noncompliant or in patients with obstruction caused by ureteric encasement or infiltration (e.g., retroperitoneal fibrosis, neoplasia). CT scanning has largely replaced retrograde pyelography through cystography or percutaneous anterograde pyelography for definitive diagnosis when obstruction without dilatation is considered

likely. The latter procedures remain useful for precise localization of the site of obstruction in selected cases and facilitate decompression of the urinary tract. Intravenous pyelography should be avoided in patients with AKI to avoid adding contrast nephropathy to already compromised renal function. Radionuclide scans have been touted as useful for assessing renal blood flow, glomerular filtration, tubule function, and infiltration by inflammatory cells in AKI; however, these tests generally lack specificity or yield conflicting or poor results in controlled studies and their use is largely restricted to the immediate postrenal transplantation period. Magnetic resonance angiography (MRA) of the kidneys is extremely useful for detecting renal artery stenosis, and its role has been extended to the evaluation of acute renovascular crises. MRA is a time-efficient and safe test when compared with conventional arteriography. Doppler ultrasonography and spiral CT are also useful in patients with suspected vascular obstruction; however, contrast angiography remains the gold standard for definitive diagnosis.

Renal biopsy is usually reserved for patients in whom cause of intrinsic AKI is not clear. Prerenal and postrenal failure should be excluded. Examples include antiglomerular basement membrane disease and other forms of necrotizing glomerulonephritis, vasculitis, HUS and

TTP, allergic interstitial nephritis, myeloma cast nephropathy, and acute allograft rejection.

NOVEL BIOMARKERS

BUN and creatinine are functional biomarkers of glomerular filtration rather than tissue injury biomarkers and, therefore, may be suboptimal for the diagnosis of actual parenchymal kidney damage. BUN and creatinine are also relatively slow to rise after kidney injury. Several novel kidney injury biomarkers have been investigated and show great promise for the early and accurate diagnosis of AKI. New biomarkers hold the promise of allowing clinicians to detect kidney injury earlier, to guide future therapy, and to better prognosticate.

Kidney injury molecule-1 (KIM-1) is a type 1 transmembrane protein that is abundantly expressed in proximal tubular cells injured by ischemia or nephrotoxins such as cisplatin. KIM-1 is not expressed in appreciable quantities in the absence of tubular injury or in extrarenal tissues. KIM-1's functional role may be to confer phagocytic properties to tubular cells, enabling them to clear debris from the tubular lumen after kidney injury. KIM-1 can be detected shortly after ischemic or nephrotoxic injury in the urine and, therefore, may be an easily tested biomarker in the clinical setting.[111]

Neutrophil gelatinase associated lipocalin (*NGAL*, also known as lipocalin-2 or siderocalin) is another leading novel biomarker of AKI. NGAL can bind to iron siderophore complexes and may have tissue-protective effects in the proximal tubule. NGAL is highly upregulated after inflammation and kidney injury and can be detected in the plasma and urine within 2 hours of cardiopulmonary bypass–associated AKI.[112-117]

MANAGEMENT OF ACUTE KIDNEY INJURY

The management of individuals with and at risk for AKI varies according to the underlying cause. Common to all are several principles. Optimization of hemodynamics, correction of fluid and electrolyte imbalances, discontinuation of nephrotoxic medications, and dose adjustment of administered medications are all critical. Common causes of AKI such as sepsis and ischemic ATN, do not yet have specific therapies once injury is established, but meticulous clinical attention is needed to support the patient until (if) AKI resolves. The kidney possesses remarkable capacity to repair itself after even severe, dialysis-requiring AKI. However, some patients with AKI do not recover fully and may remain dialysis dependent.

INDICATIONS AND MODALITIES OF DIALYSIS

Dialysis does not hasten recovery from AKI. Similarly, there is no consensus on the optimal renal replacement therapy in AKI. The preferred mode of renal replacement therapy is an area of active research. The claimed superiority of the continuous renal replacement techniques remains unproven. Neither are there evidenced-based guidelines on the initiation of dialysis in AKI. Absolute indications for the commencement of renal replacement therapy include symptomatic uremia (asterixis, pericardial rub, encephalopathy) and acidosis, hyperkalemia, or volume overload that proves refractory to medical management. However, in clinical practice, most nephrologists initiate renal replacement therapy (RRT) before the onset of overt metabolic disarray when the need for renal support appears inevitable.

The choice of dialysis modality (peritoneal dialysis, hemodialysis, or hemofiltration) is often guided by the resources of the health care institution, the technical expertise of the physician and the clinical status of the patient. The best time to start renal replacement therapy is controversial because the only studies linking timing with outcome are observational. Three forms of renal replacement therapy are available:

continuous, intermittent (either as intermittent haemodialysis or slow low efficiency dialysis), and peritoneal dialysis.

Peritoneal Dialysis

Peritoneal dialysis in AKI is effected through a temporary intraperitoneal catheter. With the development of intermittent hemodialysis, and more recently, the slow continuous blood purification therapies, there has been a decline in the use of peritoneal dialysis in the acute setting.[118-121] It is still used in the treatment of AKI in regions where access to acute intermittent or slow continuous hemodialysis is not possible. Solute clearance and control of metabolic disarray in critically ill patients may be inferior to continuous veno-venous hemofiltration, and this has been associated with an adverse outcome in infection-associated AKI.

Hemodialysis

Acute intermittent hemodialysis has been the mainstay of renal replacement therapy in AKI over the past 40 years.[122] Typically, patients undergo dialysis for 3 to 4 hours daily or on alternate days depending on their catabolic state. The major complications of acute intermittent hemodialysis relate to rapid shifts in plasma volume and solute composition, the angioaccess procedure, and the necessity for

anticoagulation. Intradialytic hypotension is common in patients undergoing acute intermittent hemodialysis.

OUTCOME

The crude mortality rate among patients with intrinsic AKI approximates 50% and has changed little over the past 3 decades. [123] Mortality rates differ markedly depending on the cause of AKI: being approximately 15% in obstetric patients, 30% in toxin-related AKI, and 60% to 90% in patients with sepsis. [124] Although it was once widely held that the provision of effective renal replacement therapy largely corrected the prognostic import of an episode of AKI, more recent observations clearly demonstrate that this is not and probably never was the case, and that all too often, the development of AKI directly contributes to poor patient outcomes. Factors associated with a poor prognosis include male sex, advanced age, oliguria (<400 mL/day), and a rise in the serum creatinine value of greater than 3 mg/dL, factors reflecting more severe renal injury and failure of other organ systems.

Even mild decreases in renal function are now recognized as being associated with worse patient outcomes. Even with the use of renal replacement therapy, mortality remains elevated as compared with those with maintained independent renal function. [125]

In addition to its clinical consequences, AKI prolongs hospital stays and is associated with substantially increased medical expenditure. [126-128]

Most patients who survive an episode of AKI regain independent renal function. However, 50% have subclinical functional defects. AKI is irreversible in approximately 5% of patients, usually as a consequence of complete cortical necrosis, and requires long-term renal replacement therapy with dialysis or transplantation. An additional 5% of patients suffer progressive deterioration in renal function after an initial recovery phase, probably because of hyperfiltration and subsequent sclerosis of remnant glomeruli.

AIMS AND OBJECTIVES

1. To study the incidence of AKI in the medical wards of our hospital
2. To study the etiological profile of AKI in medical wards
3. To apply the AKIN criteria in AKI patients admitted to the medical wards and to confirm its significance
4. To study the requirement of renal replacement therapy in AKI
5. To study the outcomes of AKI
6. To study the risk and prognostic factors of AKI

MATERIALS AND METHODS

Settings

The study was conducted at the medical wards of Govt Rajaji Hospital, Madurai.

Design of study

Cross sectional study

Period of study

6 months

Collaborating Department

Departments of Nephrology

Ethical clearance

Approval obtained from Ethical Committee headed by Dean, Govt. Rajaji Hospital, Madurai

Consent

Informed consent obtained from all patients

Data collection

Clinical and biochemical data

Conflict of interest

Nil

Financial support

Nil

TERMINOLOGY AND DEFENITIONS

AKI was defined and classified by the AKIN criteria.

Diagnostic criteria for acute kidney injury: An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours).

Classification/staging system for acute kidney injury

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dl or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg per hour for more than 6 hours
2	Increase in serum creatinine to more than 200% to 300% (> 2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours
3	Increase in serum creatinine to more than 300% (> 3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dl with an acute increase of at least 0.5 mg/dl, individuals who receive RRT)	Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours

When baseline creatinine was not available, it was derived using the four-variable MDRD equation by assuming a baseline glomerular filtration rate (GFR) of 90 mL/min/1.73 m2. Oliguric renal failure was defined as urine output <400 mL/24hrs.

Sepsis was defined as two or more of the following as a result of proven or suspected infection: (a) temperature > 38C or <36C, (b) heart rate >90/min, (c) respiratory rate >24/min, (d) W.B.C count >12,000/uL, <4000/uL, or > 10% band forms.

Tropical febrile illness was defined as fever for 5−21 days without an obvious focus of infection (such as lower respiratory tract infection or urinary tract infection).

Acute glomerulonephritis was considered in a case with clinical and biochemical markers substantiating the diagnosis.

Drugs were identified as a cause of AKI when there was a temporal relationship to administration of drugs in the absence of other pathogenic mechanisms.

Regarding the outcome, complete recovery was defined as the serum creatinine < 1.6mg/dL at the time of discharge. Partial recovery was defined as persistent dialysis-independent renal failure. The third outcome was in hospital mortality.

PATIENT POPULATION

Consecutive medical ward in-patients of GRH who were diagnosed to have AKI as per AKIN Criteria were enrolled in the study after informed consent.

EXCLUSION CRITERIA

Age < 13yrs

Pre-existing renal disease

Small contracted kidneys in USG

Obstructive uropathy

METHODS

Detailed history, clinical examination and laboratory investigation were carried out in all patients. Following important data were recorded: date when AKI was detected, date of nephrology consultation, type and frequency of dialytic support instituted. Also, exposure to nephrotoxic drugs prior to or during hospital stay, co-morbid conditions, and base line serum creatinine were noted if available. All patients were subjected to urine analysis, hemogram, blood biochemistry (which included urea, creatinine, electrolytes, calcium, and phosphorus).USG was done to rule out CKD and obstructive causes.

Renal replacement therapy (RRT) was done in patients with symptomatic uremia, serum creatinine > 4 mg/dL, fluid overload, severe metabolic acidosis and hyperkalemia unresponsive to conservative measures.

The modalities of RRT were intermittent haemodialysis (HD), and intermittent peritoneal dialysis (PD).

The outcome was assessed and all the parameters were compared with outcome.

STATISTICS

Statistical analysis was performed with Chi-square analysis. A p value < 0.05 was considered significant. Data were expressed as Mean $\pm$ 1SD.

OBSERVATIONS AND RESULTS

In this study, 112 cases of AKI were studied in the medical wards of Government Rajaji hospital, Madurai during the study period. The following observations were noted.

INCIDENCE

Of the 4304 patients admitted to the medical wards during the study period, 112 patients (2.6%) were found to have AKI as per the inclusion and exclusion criteria. The incidence of AKI in medical wards was found to be 2.6%.

PATIENT CHARACTERISTICS

The age ranges between 42.4 $\pm$ 15.55 years. Median age was 40 yrs.

Almost 50% of our patients were in the 3rd and 4th decades (Fig.1). As we have not included pre-existing CKD in our study, age group > 50 yrs have low incidence.

Out of 112 patients, 70 (62.5 %) were males while 42 (37.5%) were females (Fig.2). The sex ratio is 1.6:1

AGE AND GENDER DISTRIBUTION

	GENDER					
	FEMALE		MALE		TOTAL	
	No	%	No	%	No	%
13 - 20 yrs	0	0.0%	8	7.1%	8	7.1%
21 - 30 yrs	8	7.1%	10	8.9%	18	16.1%
31 - 40 yrs	14	12.5%	20	17.9%	34	30.4%
41 - 50 yrs	11	9.8%	12	10.7%	23	20.5%
51 - 60 yrs	4	3.6%	10	8.9%	14	12.5%
> 60 yrs	5	4.5%	10	8.9%	15	13.4%

CLINICAL FEATURES

The clinical features observed in our study were oliguria (65.2%), vomiting (61.6%), loose stools (50.9%), uremic symptoms (24.1%) breathlessness (17.9%), altered sensorium (10.7%), jaundice (9.8%), and edema (8.9%). Clinical features depend on the underlying condition and its severity.

CLINICAL FEATURES OF AKI							
		GENDER					
		FEMALE		MALE		Total	
		No.	%	No.	%	No.	%
LOOSE STOOLS	PRESENT	21	18.8%	36	32.1%	57	50.9%
VOMITING	PRESENT	26	23.2%	43	38.4%	69	61.6%
URINE OUTPUT	OLIGURIC	20	17.9%	53	47.3%	73	65.2%
	NON-OLIGURIC	22	19.6%	17	15.2%	39	34.8%
BREATHLESSNESS	PRESENT	8	7.1%	12	10.7%	20	17.9%
ALTERED SENSORIUM	PRESENT	6	5.4%	6	5.4%	12	10.7%
EDEMA	PRESENT	3	2.7%	7	6.2%	10	8.9%
UREMIC SYMPTOMS	PRESENT	8	7.1%	19	17.0%	27	24.1%
JAUNDICE	PRESENT	3	2.7%	8	7.1%	11	9.8%

URINE VOLUME

URINE VOLUME		
	Frequency	Percent
OLIGURIC	73	65.2
NON-OLIGURIC	39	34.8
Total	112	100.0

Urine volume of each patient was charted. Out of 112 patients, 73 patients (65.2%) had oliguric AKI while 39 patients had non-oliguric AKI (Fig.4).

CO-MORBIDITIES

CO-MORBIDITIES		
	Frequency	Percent
ABSENT	91	81.3
HTN	6	5.4
DM	10	8.9
CAD	3	2.7
CVA	1	.9
COPD	1	.9
Total	112	100.0

Co-morbidities were absent in 81.3% patients (Fig.5). Out of the 21 patients with co-morbidities, diabetes was present in 10 patients (8.9%), hypertension was present in 6 patients (5.4%) and CAD was present in 3 patients (2.7%). CVA and COPD were present in 1 patient each.

ETIOLOGY

The most common cause of AKI was acute diarrheal disease (50%), followed by snake bite (21.4 %), sepsis (10.7 %), tropical acute febrile illness (7.1%), and glomerulonephritis (3.6%) (Fig.6).

ETIOLOGICAL PROFILE OF AKI						
	GENDER					
	FEMALE		MALE		Total	
	No.	%	No.	%	No.	%
Acute Diarrheal Disease	20	17.9%	36	32.1%	56	50.0%
Snake Bite	8	7.1%	16	14.3%	24	21.4%
Sepsis	5	4.5%	7	6.2%	12	10.7%
Tropical Acute Febrile Illness	3	2.7%	5	4.5%	8	7.1%
Acute Glomerulonephritis	1	0.9%	3	2.7%	4	3.6%
NSAID Induced	0	0.0%	1	0.9%	1	0.9%
Super Vasmol Poisoning	3	2.7%	0	0.0%	3	2.7%
Copper Sulphate Poisoning	1	0.9%	1	0.9%	2	1.8%
Pigment Nephropathy	1	0.9%	1	0.9%	2	1.8%

ETIOLOGICAL PROFILE OF AKI : AGE WISE						
	AGE					
	13 - 20 yrs	21 - 30 yrs	31 - 40 yrs	41 - 50 yrs	51 - 60 yrs	> 60 yrs
	No.	No.	No.	No.	No.	No.
Acute Diarrheal Disease	4	8	17	10	7	10
Snake Bite	2	4	10	5	1	2
Sepsis	0	1	1	5	3	2
Tropical Acute Febrile Illness	1	0	2	2	3	0
Acute Glomerulonephritis	1	3	0	0	0	0
NSAID Induced	0	0	0	0	0	1
Super Vasmol Poisoning	0	2	1	0	0	0
Copper Sulphate Poisoning	0	0	1	1	0	0
Pigment Nephropathy	0	0	2	0	0	0

MEAN VALUES OF LABORATORY FEATURES

Characteristics	Mean	Standard deviation
Hemoglobin	9.88	1.65
Urea	97.04	48.35
Creatinine	4.59	2.96

AKIN STAGE

Of the 112 patients, 32 (28.6%), 21 (18.8%) and 59 (52.7%) were in the AKIN 1, AKIN 2 and AKIN 3 stages respectively (Fig.7).

AKIN STAGE DISTRIBUTION						
	AKIN STAGE					
	AKIN 1		AKIN 2		AKIN 3	
	No.	%	No.	%	No.	%
Acute Diarrheal Disease	17	30.4%	13	23.2%	26	46.4%
Snake Bite	8	33.3%	2	8.3%	14	58.3%
Sepsis	2	16.7%	3	25.0%	7	58.3%
Tropical Acute Febrile Illness	1	12.5%	1	12.5%	6	75.0%
Acute Glomerulonephritis	2	50.0%	1	25.0%	1	25.0%
NSAID Induced	0	0.0%	0	0.0%	1	100.0%
Super Vasmol Poisoning	2	66.7%	0	0.0%	1	33.3%
Copper Sulphate Poisoning	0	0.0%	1	50.0%	1	50.0%
Pigment Nephropathy	0	0.0%	0	0.0%	2	100.0%

TIMING OF DIAGNOSIS

DIAGNOSIS OF AKI		
	Frequency	Percent
ON ADMISSION	50	44.6
AFTER ADMISSION	62	55.4
Total	112	100.0

DIAGNOSIS OF AKI						
	AKIN STAGE					
	AKIN 1		AKIN 2		AKIN 3	
	No.	%	No.	%	No.	%
ON ADMISSION	13	26.0%	7	14.0%	30	60.0%
AFTER ADMISSION	19	30.6%	14	22.6%	29	46.8%

Of the 112 patients who developed AKI, 50 (44.6%) were detected to have AKI at the time of admission [AKIN: STAGE 1, 13 (26%); STAGE 2, 7 (14%); and STAGE 3, 30(60%)] and 62 (55.4%) developed AKI after admission [AKIN: STAGE 1, 19 (30.6%); STAGE 2, 14 (22.6%); and STAGE 3, 29 (46.8%)] (Fig.8).

MANAGEMENT

Dialysis was done as per the indications. In all, 35 patients (31.25 %) required dialytic support (Fig.9), of which 27 (24.1%) were treated by hemodialysis and 8 (7.1%) by peritoneal dialysis. The remaining 77 patients (68.8%) were treated conservatively (Fig.10). The commonest indication for dialysis was symptomatic uremia.

REQUIREMENT OF RRT				
	RRT REQUIRED			
	YES		NO	
	No.	%	No.	%
Acute Diarrheal Disease	13	23.2%	43	76.8%
Snake Bite	11	45.8%	13	54.2%
Sepsis	5	41.7%	7	58.3%
Tropical Acute Febrile Illness	2	25.0%	6	75.0%
Acute Glomerulonephritis	1	25.0%	3	75.0%
NSAID Induced	0	0.0%	1	100.0%
Super Vasmol Poisoning	1	33.3%	2	66.7%
Copper Sulphate Poisoning	0	0.0%	2	100.0%
Pigment Nephropathy	2	100.0%	0	0.0%

MANAGEMENT OF AKI						
	RRT TYPE					
	CONSERVATIVE		HEMO-DIALYSIS		PERITONEAL-DIALYSIS	
	No.	%	No.	%	No.	%
Acute Diarrheal Disease	43	38.4%	9	8.0%	4	3.6%
Snake Bite	13	11.6%	9	8.0%	2	1.8%
Sepsis	7	6.2%	3	2.7%	2	1.8%
Tropical Acute Febrile Illness	6	5.4%	2	1.8%	0	0.0%
Acute Glomerulonephritis	3	2.7%	1	0.9%	0	0.0%
NSAID Induced	1	0.9%	0	0.0%	0	0.0%
Super Vasmol Poisoning	2	1.8%	1	0.9%	0	0.0%
Copper Sulphate Poisoning	2	1.8%	0	0.0%	0	0.0%
Pigment Nephropathy	0	0.0%	2	1.8%	0	0.0%

DURATION OF HOSPITAL STAY

The mean duration of hospital stay was 9.2 $\pm$ 4.44 days.

OUTCOME

Regarding the outcome of AKI, 93 patients (83%) had complete recovery and 7 patients (6.2%) had partial recovery. The overall in-hospital mortality rate was 10.7% (Fig11).

OUTCOME OF AKI			
		No.	%
OUTCOME	COMPLETE RECOVERY	93	83.0%
	PARTIAL RECOVERY	7	6.2%
	IN-HOSPITAL MORTALITY	12	10.7%

AGE AND OUTCOME

AGE AND OUTCOME					
		OUTCOME			
		RECOVERY		IN-HOSPITAL MORTALITY	
		No.	%	No.	%
AGE	13 - 20 yrs	7	87.5%	1	12.5%
	21 - 30 yrs	18	100.0%	0	0.0%
	31 - 40 yrs	32	94.1%	2	5.9%
	41 - 50 yrs	18	78.3%	5	21.7%
	51 - 60 yrs	12	85.7%	2	14.3%
	> 60 yrs	13	86.7%	2	13.3%

P 0.278

Mortality was more in the age group of 41 –50 yrs (21.7%) while it is less in the age group of 31- 40 yrs (5.9%). So as the age advances, there is increase in mortality. Mortality appears to be less in patients above 50 years. This may be due to exclusion of CKD patients.

GENDER AND OUTCOME

GENDER AND OUTCOME					
		OUTCOME			
		RECOVERY		IN-HOSPITAL MORTALITY	
		No.	%	No.	%
GENDER	FEMALE	37	88.1%	5	11.9%
	MALE	63	90.0%	7	10.0%

P 0.849

Mortality was more in females (11.9%) than males (10.0%).

CO-MORBIDITIES AND OUTCOME

CO-MORBIDITIES AND OUTCOME				
	OUTCOME			
	RECOVERY		IN-HOSPITAL MORTALITY	
	No.	%	No.	%
ABSENT	84	92.3%	7	7.7%
HTN	6	100.0%	0	0.0%
DM	6	60.0%	4	40.0%
CAD	2	66.7%	1	33.3%
CVA	1	100.0%	0	0.0%
COPD	1	100.0%	0	0.0%

P 0.186

Among co-morbidities, mortality was more in patients with diabetes (40%) and CAD (33.3%).

ETIOLOGY AND OUTCOME

ETILOGY AND OUTCOME				
	OUTCOME			
	RECOVERY		IN-HOSPITAL MORTALITY	
	No.	%	No.	%
Acute Diarrheal Disease	55	98.2%	1	1.8%
Snake Bite	24	100.0%	0	0.0%
Sepsis	5	41.7%	7	58.3%
Tropical Acute Febrile Illness	6	75.0%	2	25.0%
Acute Glomerulonephritis	4	100.0%	0	0.0%
NSAID Induced	1	100.0%	0	0.0%
Super Vasmol Poisoning	2	66.7%	1	33.3%
Copper Sulphate Poisoning	1	50.0%	1	50.0%
Pigment Nephropathy	2	100.0%	0	0.0%

P 0.000

Sepsis induced AKI had the highest in hospital mortality of 58.3%.

URINE VOLUME AND OUTCOME

URINE VOLUME AND OUTCOME				
	OUTCOME			
	RECOVERY		IN-HOSPITAL MORTALITY	
	No.	%	No.	%
OLIGURIC	63	86.3%	10	13.7%
NON-OLIGURIC	37	94.9%	2	5.1%

P 0.039

Mortality was greater in oliguric AKI (13.7%) than in non-oliguric AKI (5.1%). This is probably due to the increased severity of the insult in oliguric AKI.

AKIN STAGE AND OUTCOME

AKIN STAGE AND OUTCOME				
	OUTCOME			
	RECOVERY		IN-HOSPITAL MORTALITY	
	No.	%	No.	%
AKIN 1	32	100.0%	0	0.0%
AKIN 2	19	90.5%	2	9.5%
AKIN 3	49	83.1%	10	16.9%

P 0.007

Mortality in AKIN stages were 0.0%, 9.5%, and 16.9% respectively for stage 1, stage 2 and stage 3. Thus, as the severity of AKI increases, mortality also increases.

TIMING OF DIAGNOSIS AND OUTCOME

TIMING OF DIAGNOSIS AND OUTCOME				
	OUTCOME			
	RECOVERY		IN-HOSPITAL MORTALITY	
	No.	%	No.	%
ON ADMISSION	45	90.0%	5	10.0%
AFTER ADMISSION	55	88.7%	7	11.3%

P 0.969

Mortality was more in patients who developed AKI after admission to hospital (11.3%)

DIALYSIS REQUIREMENT AND OUTCOME

DIALYSIS REQUIREMENT AND OUTCOME					
		OUTCOME			
		RECOVERY		IN-HOSPITAL MORTALITY	
		No.	%	No.	%
RRT REQUIRED	YES	30	85.7%	5	14.3%
	NO	70	90.9%	7	9.1%

P 0.000

Mortality is more in patients who underwent dialysis (14.3%) than in patients who were treated conservatively (9.1%). Thus dialysis does not improve the outcome of patients with AKI.

DISCUSSION

INCIDENCE

The incidence of AKI is difficult to estimate because no registry of its occurrence exists and because up until recently there was no standardized definition. From a variety of predominantly single centre studies it is estimated that 5% to 7% of hospitalized patients develop AKI.[33-36]

In our study, the incidence of AKI was 2.6%. This is in concordance with a previous study done by **Kaul et al**[129] in North India in which the incidence of AKI was 2.5%.

AGE

Almost 50% of our patients were in the 3rd and 4th decades. Age group 13 to 20 yrs had the least incidence. The mean age of the population was 42.4 $\pm$ 15.55 years. Median age was 40 yrs. Only 13.4% patients were more than 60 yrs of age. This implies the occurrence of AKI in the younger age groups as compared with developed countries. In a country like India where access to health care insurance is limited, AKI in middle aged population creates a huge economic burden on the families.

SEX

In our study, out of 112 patients, 70 (62.5 %) were males while 42 (37.5%) were females.

CLINICAL FEATURES

The common clinical features were oliguria (65.2%), vomiting (61.6%), loose stools (50.9%), and uremic symptoms (24.1%). Edema was the least common symptom present in 8.9%. This means that most of our patients presented early in the course of illness. This also reflects the adequacy of referral services.

Based on urine volume, patients were classified into oliguric and non-oliguric groups. In our study, oliguric AKI predominates (65.18%). This is in concordance with a previous study **Muthusethupathi et al**.[130]

CO-MORBIDITIES

Co-morbidities were present in 18.7% of patients. Diabetes was the commonest (8.9%), followed by hypertension (5.4%) and CAD (2.7%).

ETIOLOGY

Acute diarrhoeal disease was the leading cause of AKI in our study accounting for 50 % of cases. This is despite an improvement in hygiene, socioeconomic and living conditions and a greater stress on rehydration therapies. This may be in part due to a lack of awareness on the part of

general practitioners, delays in correction of fluid and electrolyte losses, and late referral.[18]Although there seems to be a decline in AKI due to diarrhoeal disease reported from other centers,[18] such a pattern was not observed here.

In our study, AKI due to ADD was most common in the 3rd decade (30.3%). Males (64.2%) were commonly affected by ADD than females. Because they are the bread winners of the family, they are used to consuming outside food.

AKIN stage distribution of ADD: Stage 1, 17(30.4%); Stage 2, 13(23.2%); Stage 3, 26 (46.4%).

Of 56 patients with AKI due to ADD, 13 (23.2%) were treated with dialysis. The remaining 43 patients (76.8%) were treated conservatively. The mortality observed during the study was 1.8%.

Jayakumar et al[132] in their study from Chennai reported that ADD was the commonest cause of AKI (28.6%). The mortality was 8.7% and requirement of RRT was 66.1%.

Kaul et al[129] in their study reported that 29 % cases of AKI in North India were due to diarrhoeal diseases. Mortality was 14.8% and requirement of RRT was 72.2%.

AKI following snake bite is a major problem in rural India, contributing to 21.4 % of AKI cases in our study. This is comparable to other reported series from India (13-32%).[444]

AKI due to snake bite also was also common in the 3rd decade (41.6%) and in males (66.6%). Males are the bread winners of the family. They indulge in agricultural work without adequate use of protective footwear. This may be reason for the above finding.

AKIN stage distribution of snake bite: Stage 1, 8(33.3%); Stage 2, 2(8.3%); Stage 3, 14 (58.3%).

Of the 24 patients with snake bite AKI, 11(45.8%) were treated with dialysis. There was no mortality observed during the study.

Athappan et al[133] in their study from Madurai reported the prevalence of AKI in snake bite to be 13.5%. In this study, the requirement of RRT was 45.3% and the mortality observed was 22.5%. According to this study, the risk factors for development of AKI were cellulitis and regional lymphadenopathy, while the predictors of poor outcome were hypotension and bleeding.

Sweni et al[134] in their study from Chennai reported a prevalence of AKI in snake bite of 7%.

Jayakumar et al[132] in their study reported that 7.8% of cases of AKI were due to snake bite. The requirement of RRT in this study was 94.2%. As the study was done in a tertiary referral centre, most patients were referred late with renal failure. They reported a mortality of 27.5%.

Sepsis is the emerging cause of AKI. It accounted for 10.7% of cases of AKI in our study. AKI due to sepsis were common in the 4^{th} (41.6%) and 5^{th} decades (25%).

AKIN stage distribution of sepsis induced AKI: Stage 1, 2(16.7%); Stage 2, 3(25%); Stage 3, 7 (58.3%).

Sepsis induced AKI had the highest in-hospital mortality of 58.3%, which is similar to data from other Indian centres. It may be due to an association with co-morbid illnesses (Diabetes), and higher incidence of multi organ dysfunction syndrome in these patients. Thus sepsis- induced AKI was among the worst prognostic group.

Worldwide, the incidence of sepsis related AKI is increasing. AKI represents an independent risk factor for mortality in these patients. The requirement of dialysis in our study was 41.7%.

Jayakumar et al[132] reported the incidence of sepsis related AKI to be 8.8%. The requirement of RRT was 78.5% and mortality was 56.1%.

Kaul et al[129] reported a mortality of 46.1% and need for dialysis of 92.3% for sepsis related AKI.

Tropical acute febrile illnesses are a common cause of AKI in the developing countries. In Southern India, the common tropical acute febrile illness among hospitalized patients included malaria, typhoid, scrub typhus, dengue, leptospirosis, spotted fever and others. In our study, tropical acute febrile illnesses accounted for 7.14% of AKI. Out of 8 patients, 6 (5.3%) were due to leptospirosis. For the remaining 2 patients (1.7%) the aetiology of fever could not be ascertained.

AKIN stage distribution of tropical acute febrile illness induced AKI: Stage 1, 1(12.5%); Stage 2, 1(12.5%); Stage 3, 6 (75%).

Two patients (25%) with leptospirosis required dialysis, both had in-hospital mortality (25%).

Basu et al[135] in a study from Vellore reported a 3.9 % incidence of AKI in leptospirosis. There was no mortality or requirement for dialysis. The incidence of leptospirosis in this study was lower than that observed in centres with humid, marshy environment and higher rainfall.[136]

Jayakumar et al[132] reported a 7.5% incidence of AKI in leptospirosis. 53.5% of patients required dialysis and mortality was 9.5%.

Kaul et al[129] reported an incidence of 6.25% of leptospirosis related AKI.

There has been a dramatic reduction in the incidence of leptospiral AKI. Leptospirosis was once the most common cause of AKI in this part of India[130]. Whether this reduced incidence is real or due to greater awareness, better diagnostic facilities, and/or the widespread use of empirical penicillin is not clear.

In the last decade, malaria has returned to many places from where it was said to have been eradicated. India contributes 80% of all cases of malaria in Southeast Asia. Although falciparum infection remains the most common cause of complicated malaria, various Indian investigators have documented the increased incidence of complicated malaria in vivax infections. AKI due to falciparum malaria has been reported mostly from Southeast Asia and Africa. Malarial AKI has not been reported in the current study.

No cases were also reported by **Muthusethupathi et al**[130].

Jayakumar et al[132] reported a 4.4% incidence of AKI, mostly (93.8%) due to plasmodium falciparum. Plasmodium vivax was also observed in 6.2% of malarial AKI. Dialysis was required in 77.5% and mortality was 26.5%.

Kaul et al[129] reported an incidence of malarial AKI of 18.8%. Need for dialysis was 88.6% and mortality was 20%.

Basu et al[135] in their study reported that falciparum malaria (pure and mixed, respectively) had the highest incidence of AKI (63.2% and 54.2%). Mortality was much lower (13.2% and 4.2%) compared with the other acute febrile illnesses. Requirement of RRT was 23.7% and 16.7% respectively. Probably due to early diagnosis and effective treatment, the mortality was much lower. All patients who died had AKI, making it an important risk factor for mortality.

In our study, 4 patients (3.6%) had acute glomerulonephritis. AKI due to AGN is most common in the 3rd decade (75%).

AKIN stage distribution of AGN induced AKI: Stage 1, 2(50%); Stage 2, 1(25%); Stage 3, 1 (25%).

One patient was treated with HD (25%). All patients recovered.

Jayakumar et al[132] reported the incidence of AGN related AKI to be 9.3%. The requirement of RRT was 84.6% and mortality was 21.1%. Crescentic glomerulonephritis, followed by post-infectious proliferative glomerulonephritis, SLE, and IgA nephropathy (in order of frequency), accounted for the cases.

Kaul et al[129] reported an incidence of AGN related AKI of 6.45%. Need for dialysis was 66.7% and mortality was 25%.

Drugs are a common cause of AKI. In our study only patient (0.9%) had NSAID induced AKI. He was managed conservatively.

Jayakumar et al[132] reported that drugs were the second most common cause of AKI. Unknown analgesic combinations were the most common reason for admission due to drug-induced AKI, followed by Rifampicin and NSAIDS. Rifampicin-induced AKI was noted to occur frequently in patients who received intermittent therapy.

Kaul et al[129] reported an incidence of drug induced AKI of 6.45%. Need for dialysis was 77.8% and mortality was 22.2%.

AKI due to Super Vasmol poisoning contributed 2.7% and that due to copper sulphate poisoning contributed 1.8% in our study. All cases of Super Vasmol poisoning occurred in females. Suicidal tendency is more common in females than in males.

Among 3 patients with Super Vasmol poisoning, one required dialysis in the form of HD (33.3%). The patient however had in-hospital mortality (33.3%). Among 2 patients with copper sulphate poisoning, both were treated conservatively, however one patient had in-hospital

mortality. There were no cases of AKI due to rat killer poison in our study.

Super Vasmol is now emerging as a major cause of suicidal poisoning in India.[137] **Sahay et al**[138] reported that 0.6% of all AKI in their study was due to Super Vasmol.

Sweni et al[134] reported that amongst the chemical poisons, copper sulphate (10%) and rat killer (1.4%) were the commonest causes of AKI.

Jayakumar et al[132] in their study reported an incidence of 4.3% for copper sulphate induced AKI with a requirement of dialysis of 64.5% and mortality of 35.4%.

No cases of Super Vasmol poisoning were reported by **Jayakumar et al**[132] and **Kaul et al**.[129]

2 patients (1.8%) with AKI in our study were due to pigment nephropathy. Both patients required RRT in the form of HD. Both patients recovered.

TIMING OF DIAGNOSIS

55.4% patients developed AKI after admission. This may be due to two reasons. Either our treatment was ineffective, or we paid much attention to renal parameters.

44.6% of patients had AKI on admission. Measures should be aimed at prevention of AKI. They are best initiated at the community and primary healthcare level rather than at a tertiary hospital level.

DIALYSIS

Literature regarding the modality of choice for dialysis is conflicting. There is no study which has conclusively demonstrated the appropriate type and dose of RRT in AKI.[139] The percentage of patients with AKI who required dialysis was 31.25 %.

Among the common causes of AKI, the requirement of dialysis was more with snake bite (45.8%) than with ADD (23.2%). Thus snake bite needs more intensive treatment than ADD because of infection, hemolysis and anemia.

Of the dialytic modalities, hemodialysis was the most commonly used. 27 patients (24.1%) were treated by hemodialysis. Peritoneal dialysis was used in 8 patients (7.1%). Although HD is the dialytic modality of choice in many centres, PD because of its easy availability and low cost remains a major dialytic modality in many hospitals. PD can also be used as a bridge therapy, avoiding the use of central catheters which can cause infectious complications.

OUTCOME

Mortality rates in AKI are variable, ranging from approximately 7% among patients admitted to a hospital with prerenal AKI to more than 80 percent among patients with postoperative AKI.[140] Mortality rate among patients with AKI have not decreased appreciably, despite major advances in dialysis and intensive care.[141]This phenomenon can be explained by two demographic changes. Age of the patients is continuing to rise and increased incidence of coexisting serious illnesses among these patients. Most common causes of death with the advent of dialysis are sepsis, cardiopulmonary dysfunction, and the withdrawal of life-support measures.[140]

In our study, 93 patients (83%) had complete recovery and 7 patients (6.2%) had partial recovery. The in-hospital mortality in our study was 10.7%. In our study, mortality was more in patients in the fourth decade and in females. However both associations were not statistically significant.

Among co-morbidities diabetes (40%) and CAD (33.3%) were associated with high mortality. This association was also not statistically significant.

Mortality was greater in oliguric AKI (13.7%) than in non-oliguric AKI (5.1%). This is probably due to the increased severity of the insult in oliguric AKI. Thus in our study, oliguric AKI was an independent risk factor for mortality. This is concordant with many other studies.[142]

Sepsis induced AKI had the highest in-hospital mortality rate of 58.3%. Among the general public, there is wide spread belief in non qualified and indigenous practitioners and quacks. There is also lack of medical facilities in rural areas. Along with poverty, these factors lead to delayed presentation of the patient to hospital with multiorgan dysfunction and sepsis which is associated with very high mortality.

Mortality in AKIN stages were 0.0%, 9.5%, and 16.9% respectively for stage 1, stage 2 and stage 3. Thus, as the severity of AKI increases, mortality also increases.

Mortality was more in patients who were diagnosed to have AKI after admission (11.3%) than in patients who were diagnosed on admission (10%).

Mortality was more in patients who underwent dialysis (14.3%) than in patients who were treated conservatively (9.1%). Thus dialysis does not improve the outcome of patients with AKI. Although it was once widely held that the provision of effective renal replacement therapy

largely corrected the prognostic importance of an episode of AKI, more recent observations clearly demonstrate that this is not and probably never was the case, and that all too often, the development of AKI directly contributes to poor patient outcomes. Even mild decreases in renal function are now recognized as being associated with worse patient outcomes. Even with the use of renal replacement therapy, mortality remains elevated as compared with those with maintained independent renal function. [125]

Mortality in patients with AKI were known to be high with coma, assisted respiration, hypotension, jaundice, prolonged renal failure, high entry serum creatinine, hypoalbuminemia, anemia, sepsis, severe co-morbidities, multiorgan failure, and oliguria[12.] **Jayakumar et al**[132] reported oliguria, high entry serum creatinine (>440 μmol), jaundice, sepsis, anemia, and hypoalbuminemia to be risk factors associated with mortality.

AKI is a significant risk factor for mortality in these patients. Stratification based on the AKIN staging clearly demonstrates an incremental risk of primary end points such as mortality and RRT requirement. AKIN criteria, initially framed for ischemic AKI and

validated in the western world among critically ill hospitalized patients,[143] are equally valid and applicable to AKI in our setting. Apart from increased mortality, longer duration of hospital stay and the requirement of renal replacement therapy, the loss of the young workforce increases the economic burden. Using these criteria, it is now possible to identify patients at an early stage of AKI and study effective therapeutic or preventive measures. This can contain and prevent AKI, reducing morbidity and mortality, saving money and lives.

CONCLUSIONS

1. The incidence of AKI in the medical wards of G.R.H, Madurai was 2.6%. The incidence correlates well with other studies.
2. Clinical spectrum of AKI:
    - Most common age group was 30 to 40 yrs in this study
    - The incidence of AKI was more in males than females (1.6:1 ratio)
    - Most common clinical features were oliguria (65.2%), vomiting (61.6%) and loose stools (50.9%)
    - Co-morbidities found in the decreasing order were DM, HTN and CAD
    - Oliguric AKI and non-oliguric AKI were seen in 65.2 % and 34.8% respectively
3. Etiology of AKI: Acute diarrheal disease (50%) was the most common cause of AKI, followed by snake bite (21.4 %), sepsis (10.7%), tropical acute febrile illness (7.1%), glomerulonephritis (3.6%).
    - Acute diarrhoeal disease still remains the most common cause of acute kidney injury. Mortality observed during the study is very low when compared the previous studies. Awareness of

early rehydration therapy and early referral to higher centres contributed to decline in mortality.

- Snake bite induced AKI is very high in our study compared to other studies
- Leptospiral AKI is on the decline. Drugs and sepsis are emerging causes of AKI

4. According to AKIN Criteria, 28.6%, 18.8% and 52.7% were in the AKIN 1, AKIN 2 and AKIN 3 stages respectively.
5. 44.6% of patients were detected to have AKI on admission while 55.4% developed AKI after admission.
6. Requirement of dialytic support in our study was 31.25%, of which 24.1% were treated by hemodialysis and 7.1% by peritoneal dialysis.
7. Hemodialysis has become the preferred mode of renal replacement therapy.
8. Outcome:
    - Complete recovery was seen in 83% cases and partial recovery was seen in 6.2% cases
    - In-hospital mortality rate was 10.7%
    - Sepsis induced AKI had the highest in-hospital mortality (58.3%)

9. Risks and prognostic factors

    - Oliguric AKI was associated with increased mortality
    - Higher AKIN stage was associated with increased mortality
    - Dialysis requirement was associated with increased mortality

Figure 1

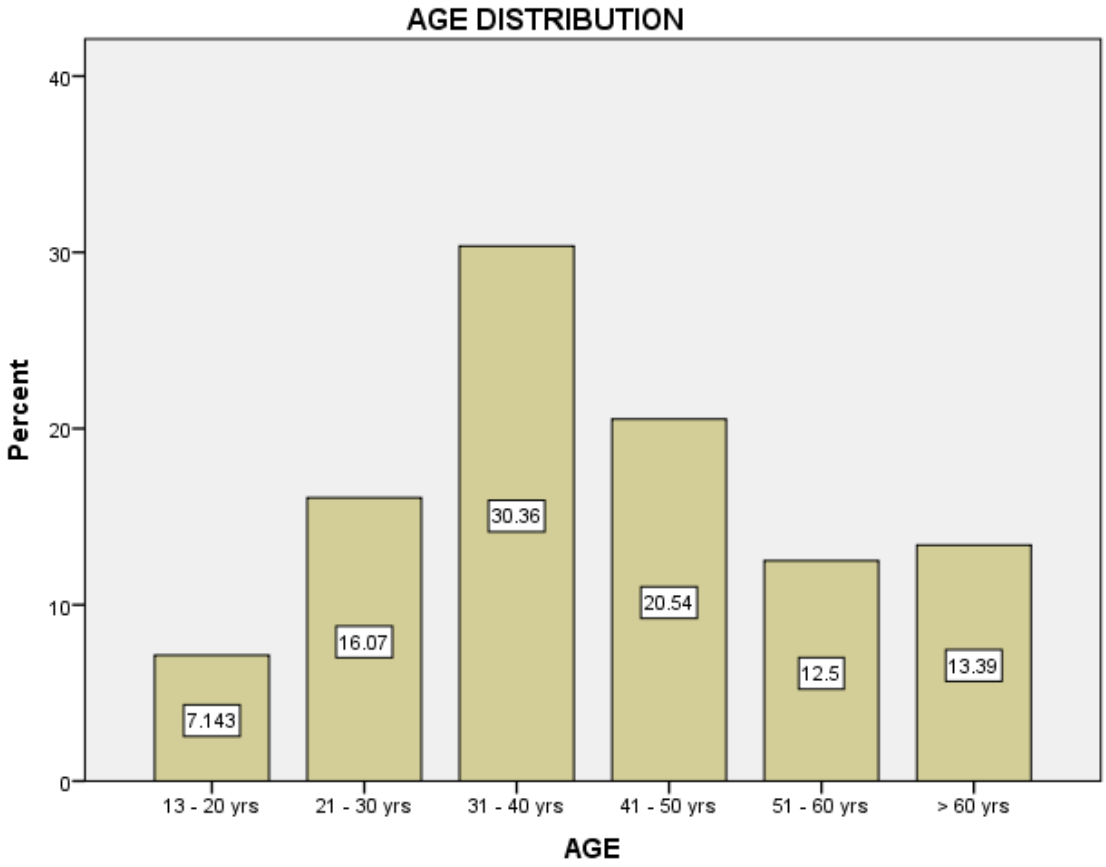


Figure 2

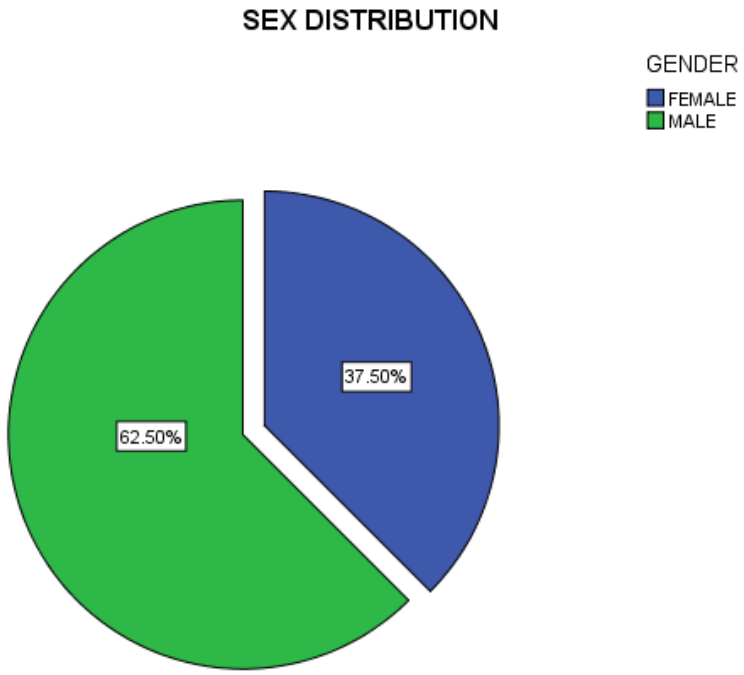
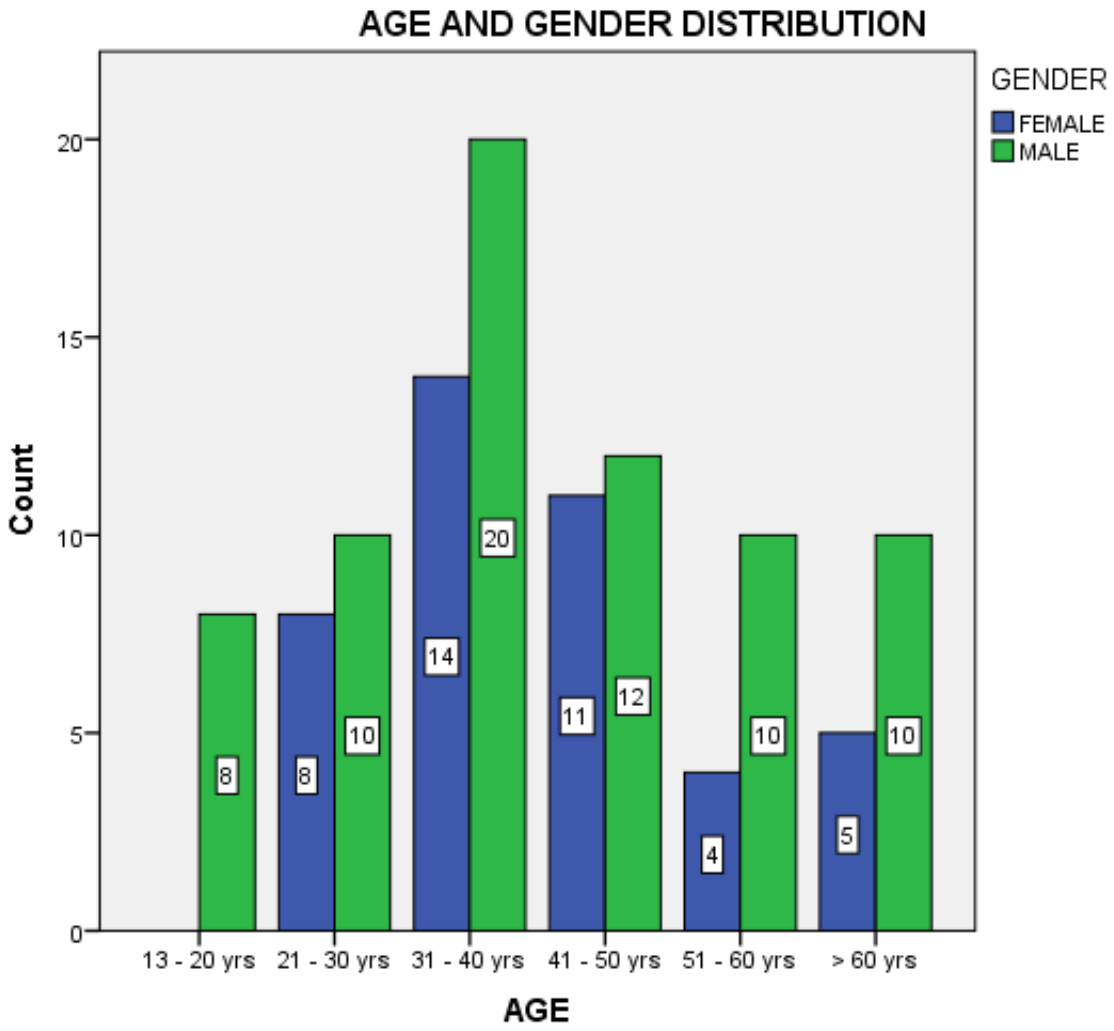


Figure 3


AGE AND GENDER DISTRIBUTION
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4
10
5
10
13 - 20 yrs
21 - 30 yrs
31 - 40 yrs
41 - 50 yrs
51 - 60 yrs
> 60 yrs
AGE

Figure 4

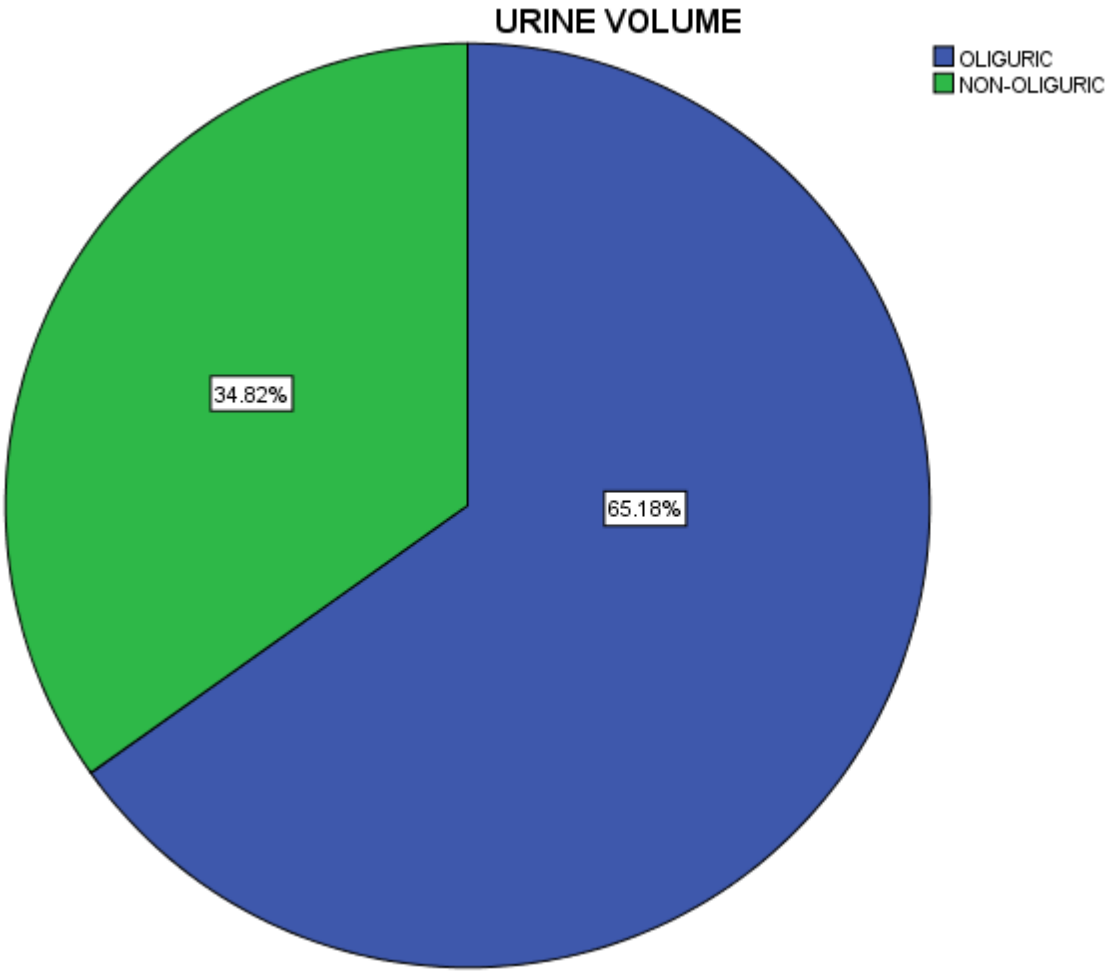


Figure 5

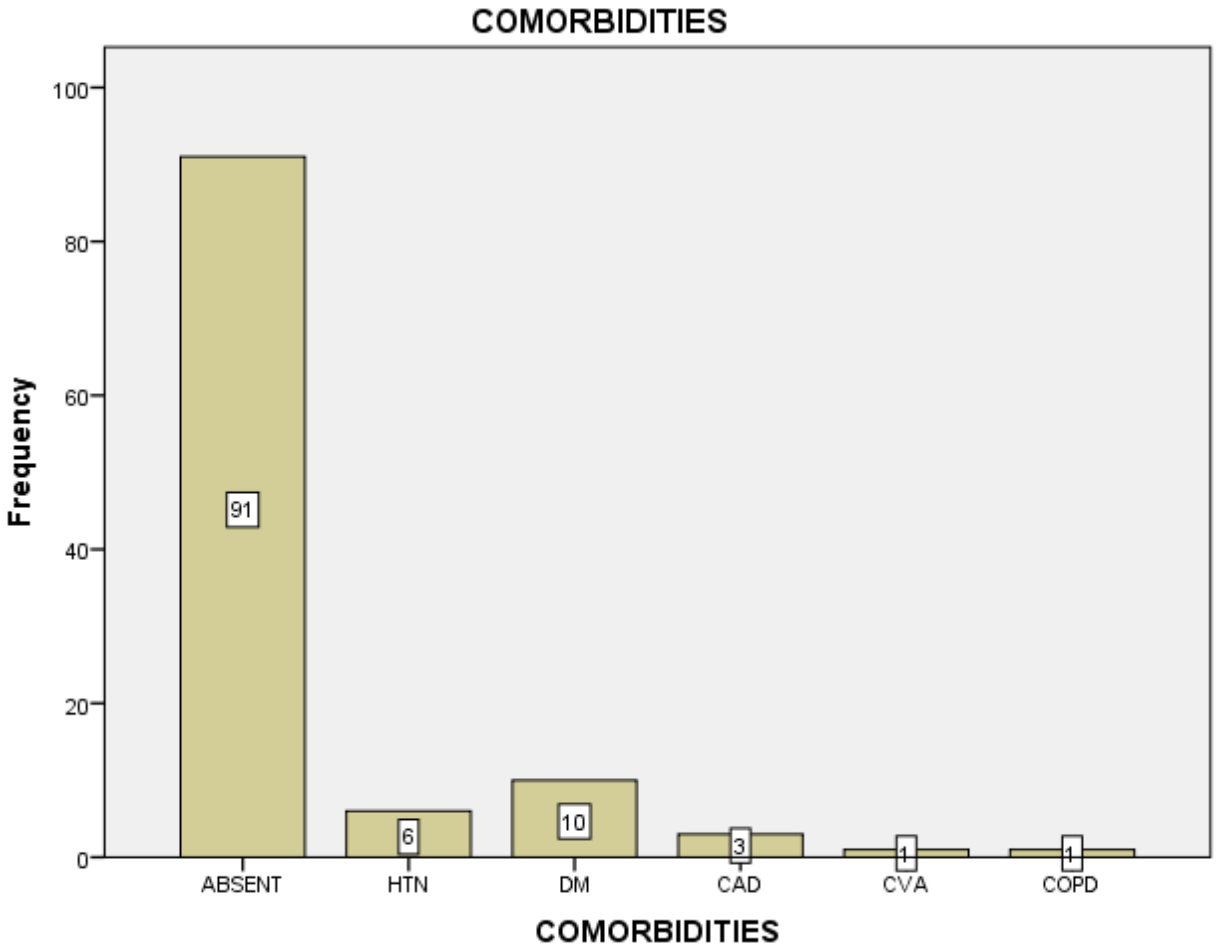

COMORBIDITIES
Frequency
100
80
60
40
20
0
91
6
10
3
1
1
ABSENT
HTN
DM
CAD
CVA
COPD
COMORBIDITIES

Figure 6

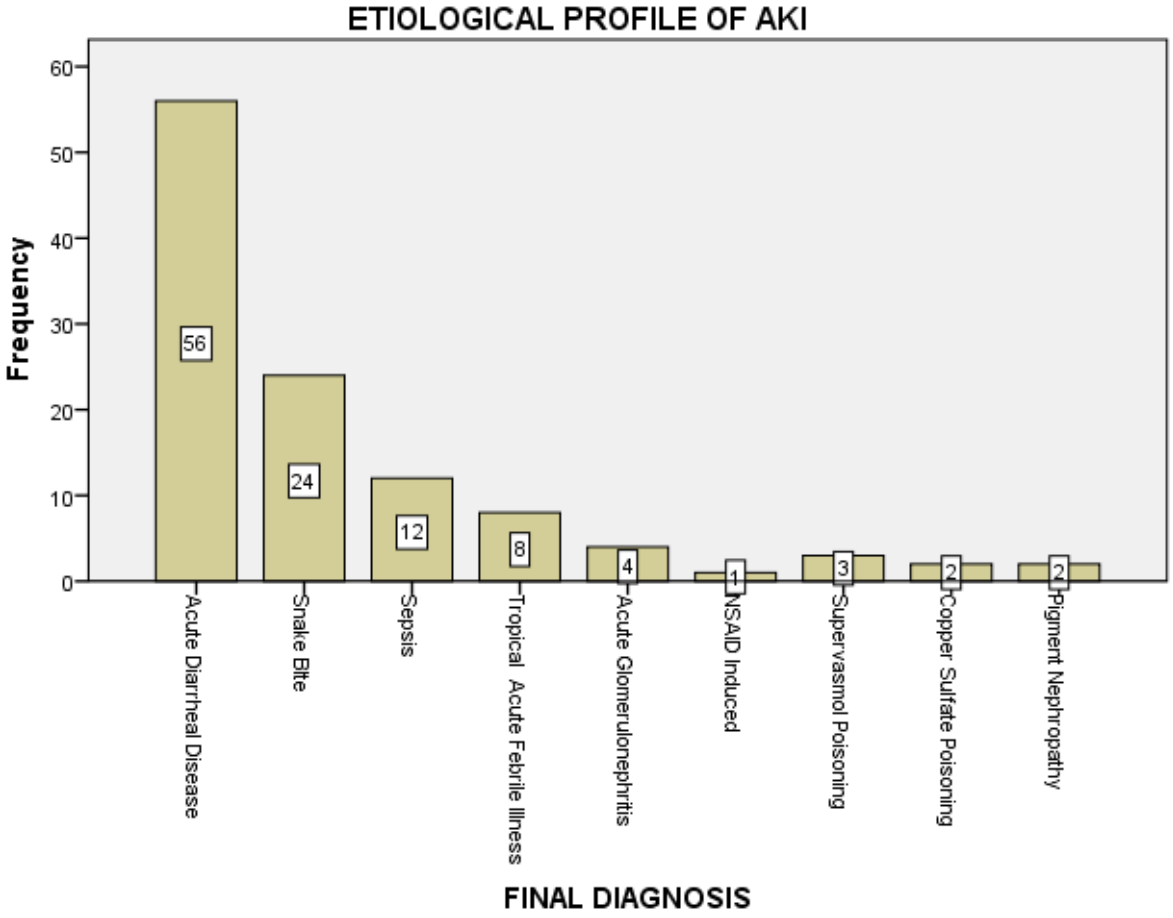

ETIOLOGICAL PROFILE OF AKI
Frequency
60
50
40
30
20
10
0
56
24
12
8
4
1
3
2
2
Acute Diarrheal Disease
Snake Bite
Sepsis
Tropical Acute Febrile Illness
Acute Glomerulonephritis
NSAID Induced
Supervasmol Poisoning
Copper Sulfate Poisoning
Pigment Nephropathy
FINAL DIAGNOSIS

Figure 7

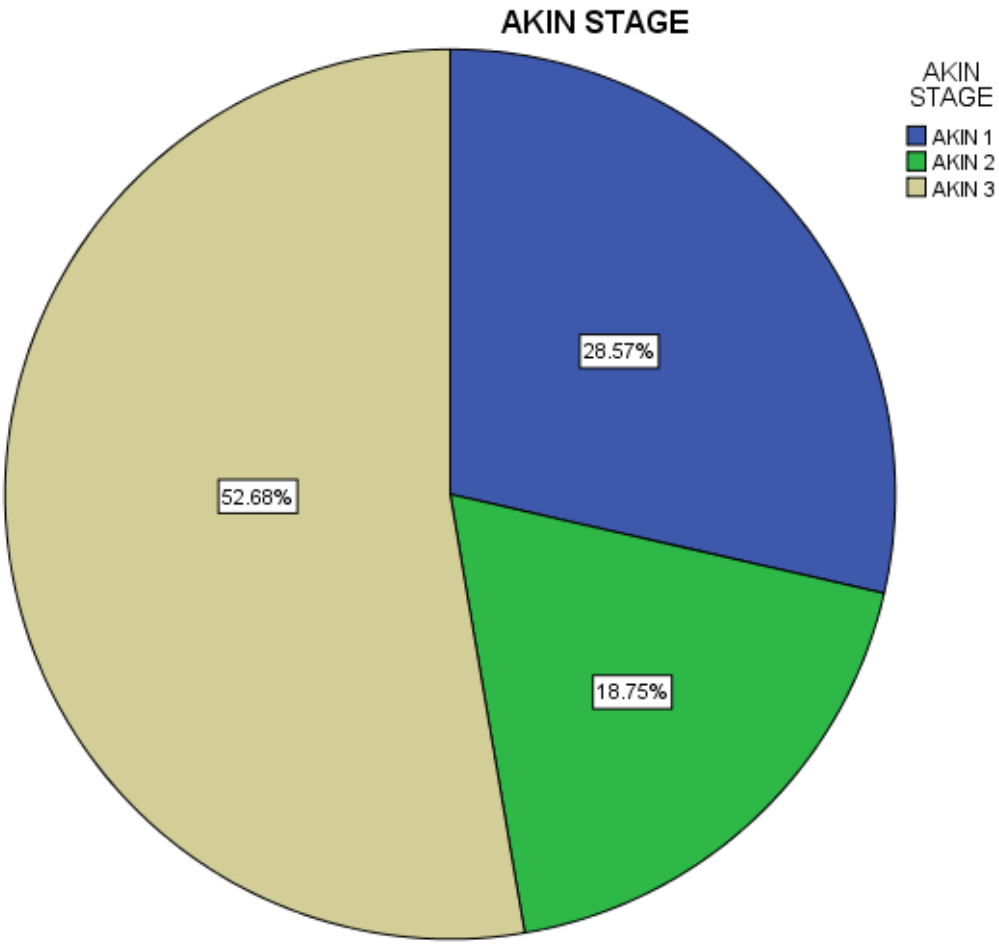


Figure 8

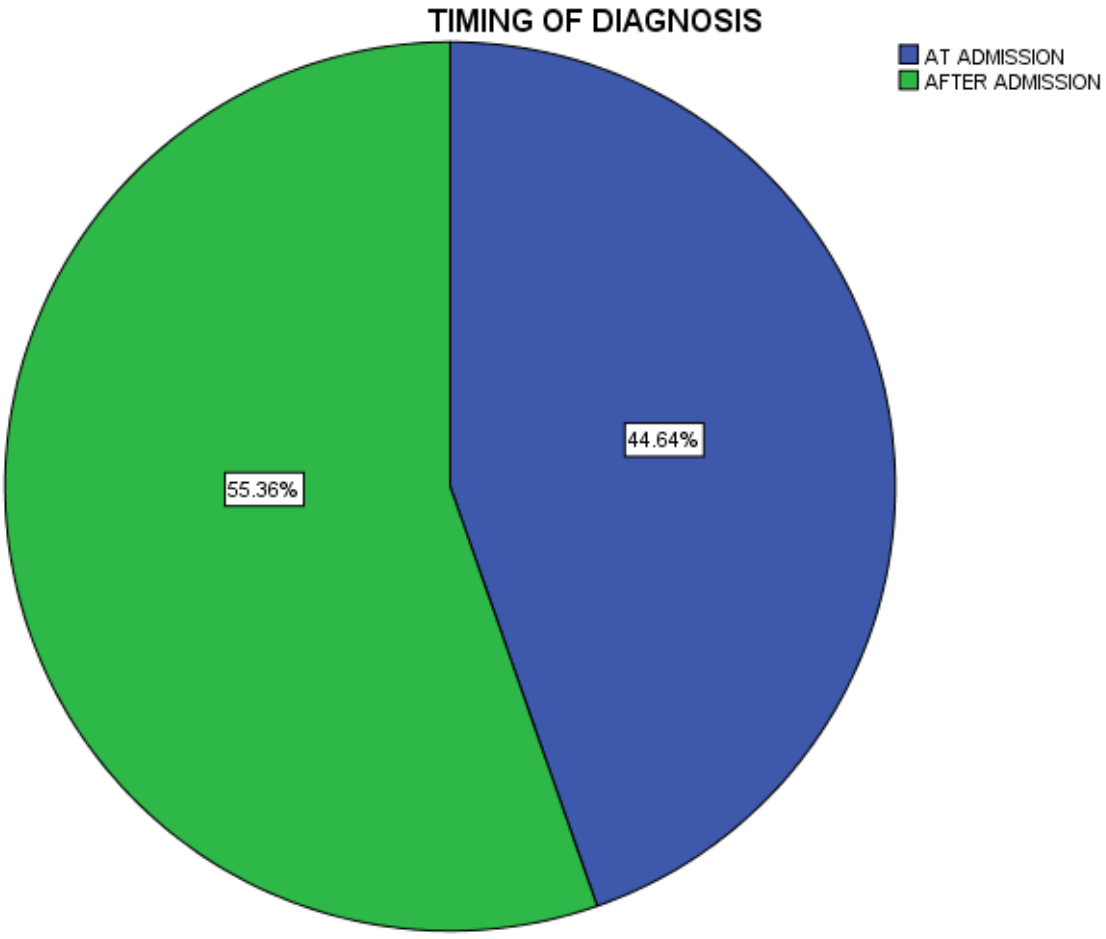

TIMING OF DIAGNOSIS
AT ADMISSION
AFTER ADMISSION
44.64%
55.36%

Figure 9

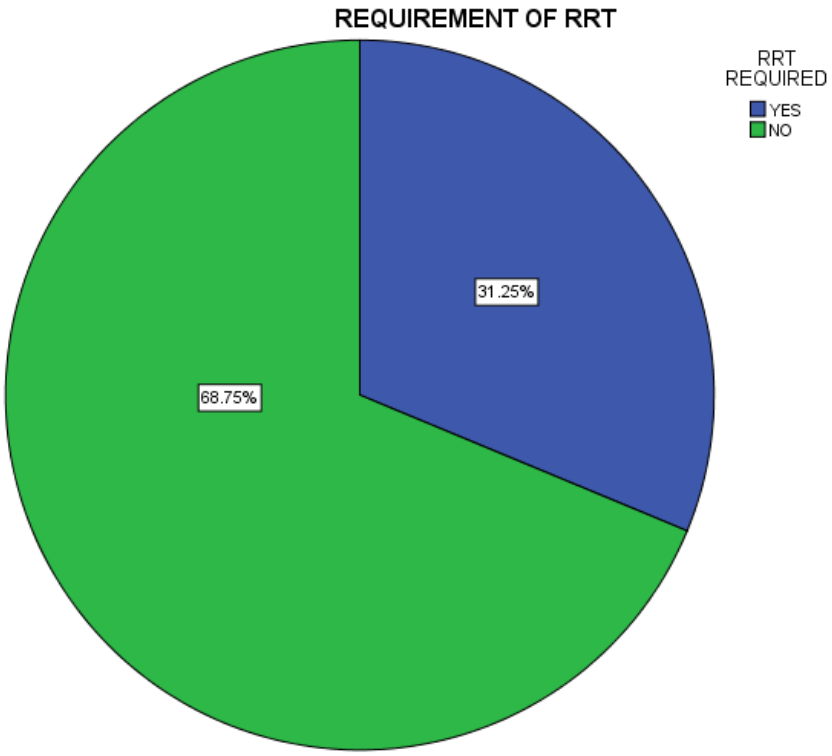


Figure 10

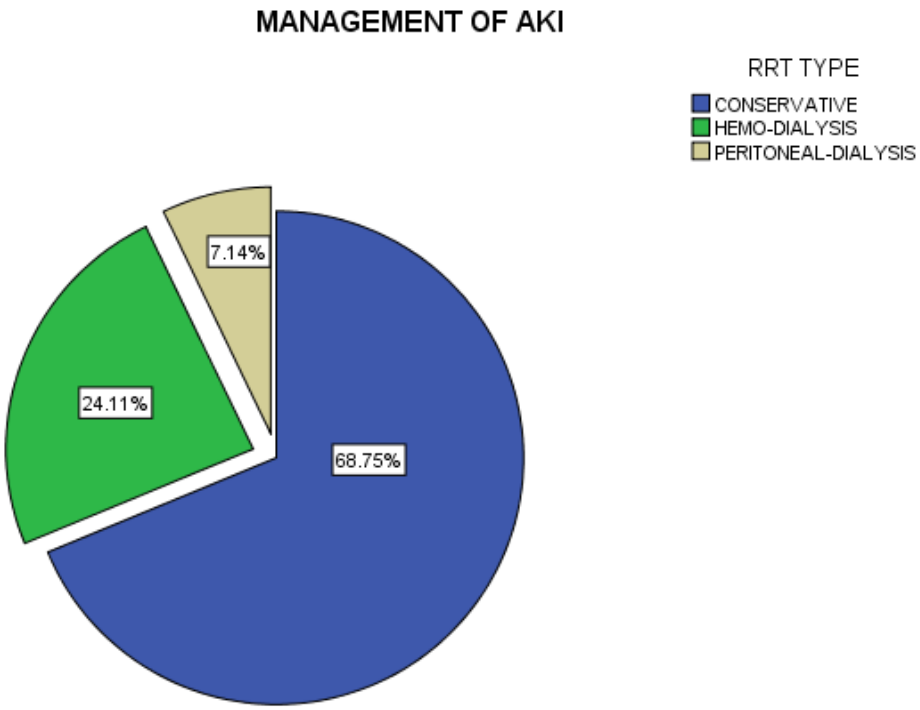

MANAGEMENT OF AKI
RRT TYPE
CONSERVATIVE
HEMO-DIALYSIS
PERITONEAL-DIALYSIS
7.14%
24.11%
68.75%

Figure 11

OUTCOME OF AKI

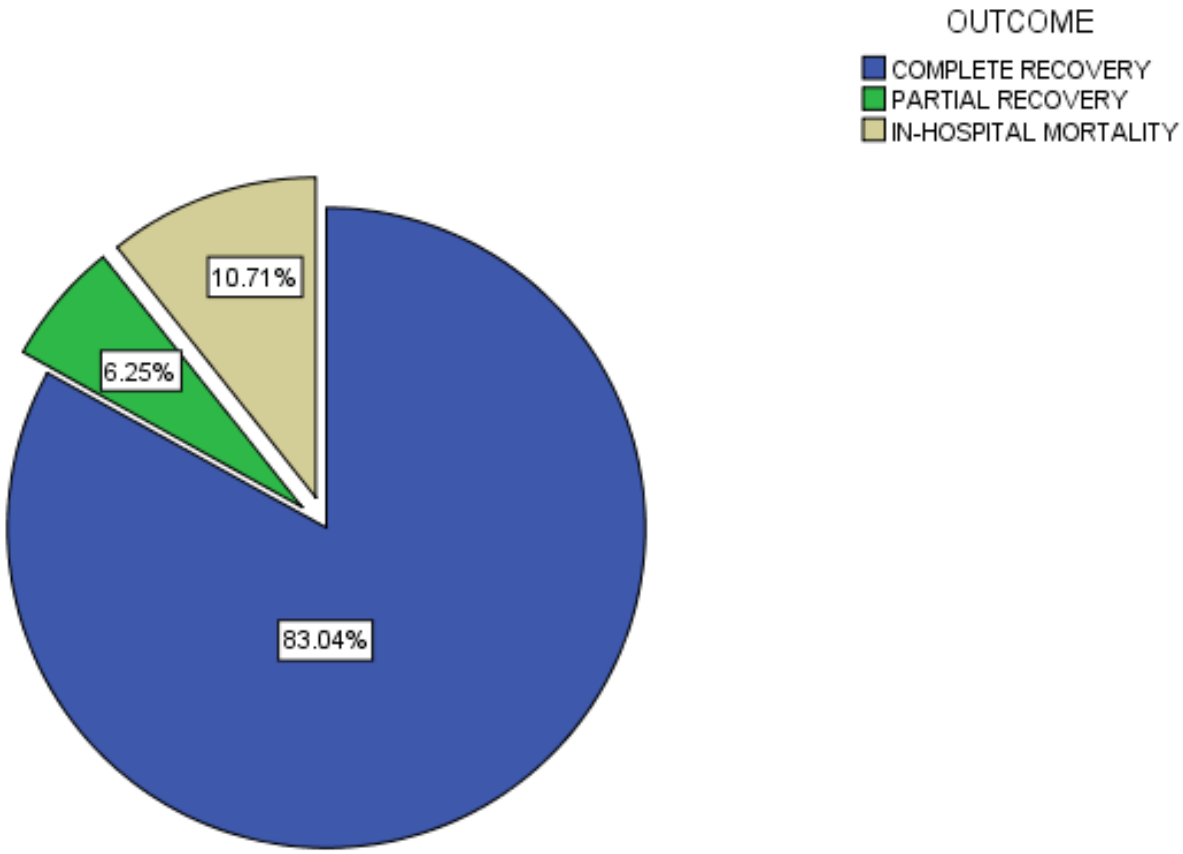
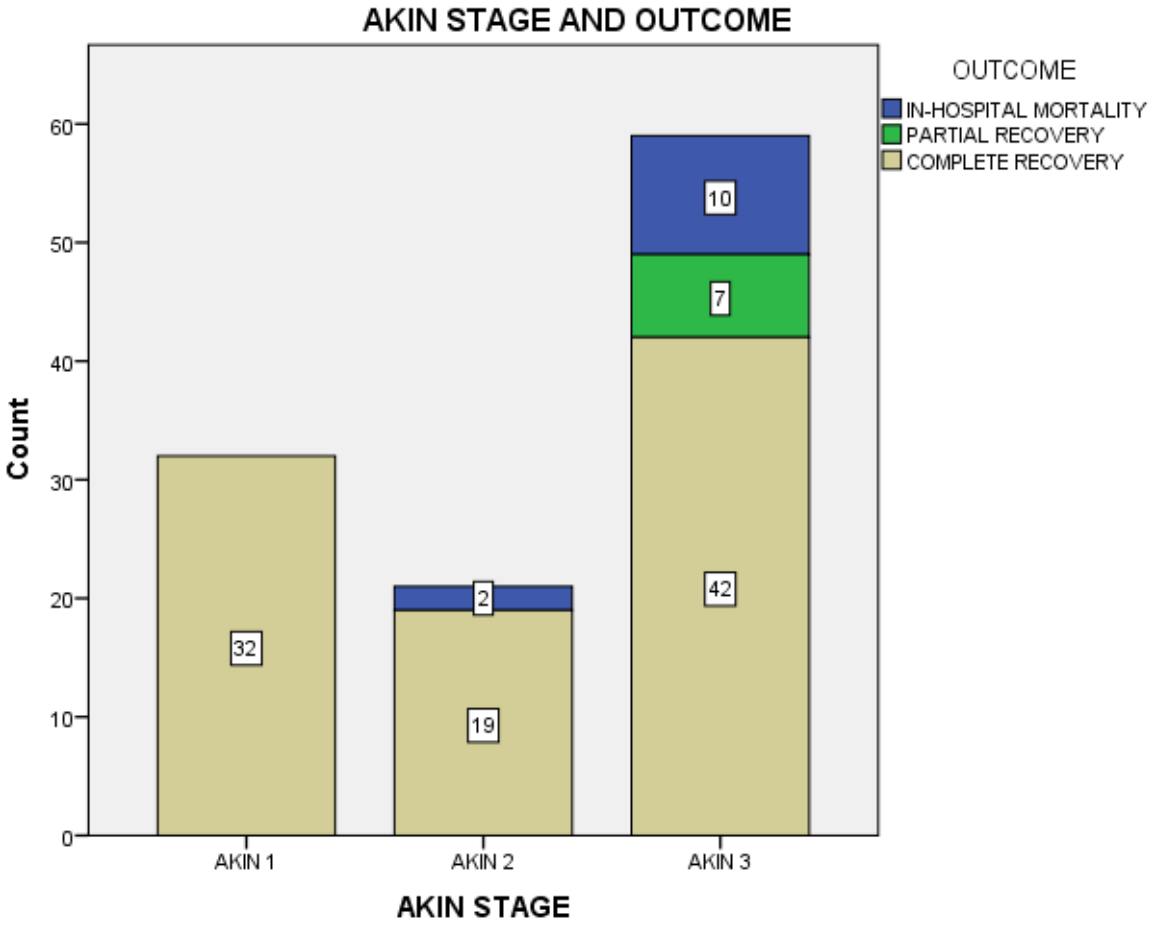
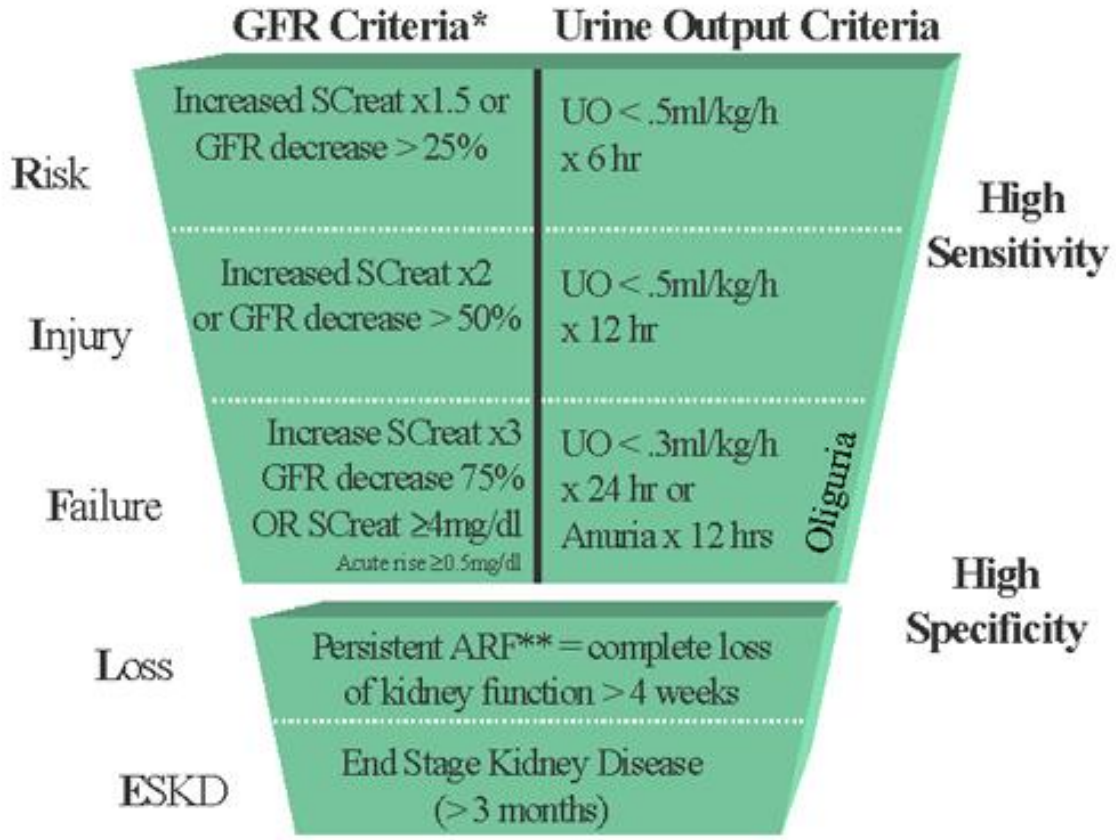
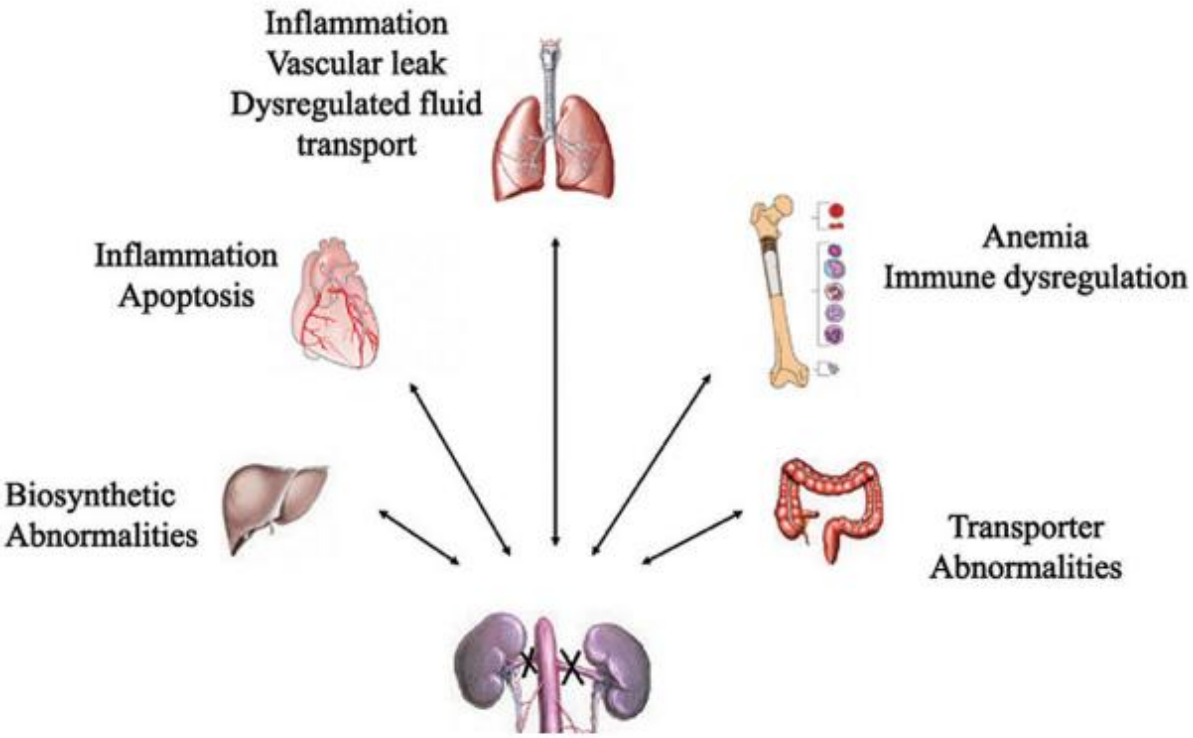


Figure 12

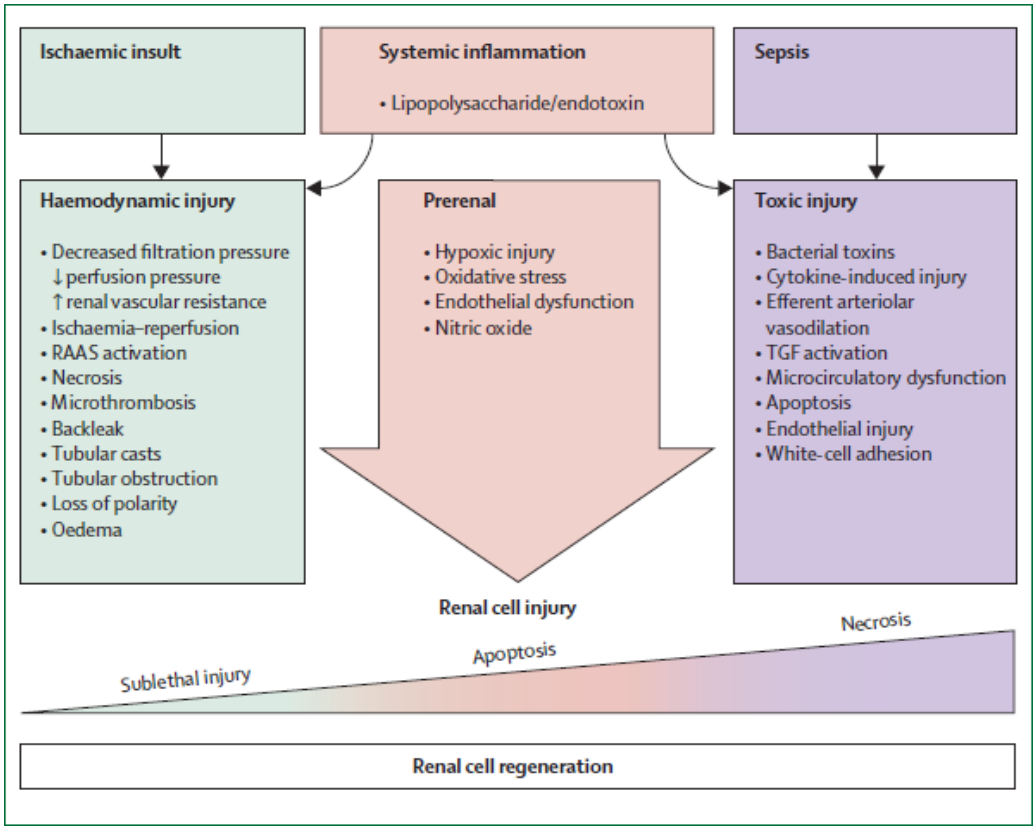

AKIN STAGE AND OUTCOME
OUTCOME
IN-HOSPITAL MORTALITY
PARTIAL RECOVERY
COMPLETE RECOVERY
Count
60
50
40
30
20
10
0
10
7
42
2
19
32
AKIN 1
AKIN 2
AKIN 3
AKIN STAGE



RIFLE classification scheme for acute renal failure. The classification system includes separate criteria for creatinine and urine output. A patient can fulfill the criteria through changes in serum creatinine (SCreat) or changes in urinary output, or both. The criteria that lead to the worst possible classification should be used.



Organ cross-talk: Distant organ effects following ischemic acute kidney injury. Organ cross-talk can include the liver, heart, lungs, bone marrow, and gastrointestinal tract.



Key potential pathways implicated in pathogenesis of acute kidney injury due to ischaemia or sepsis

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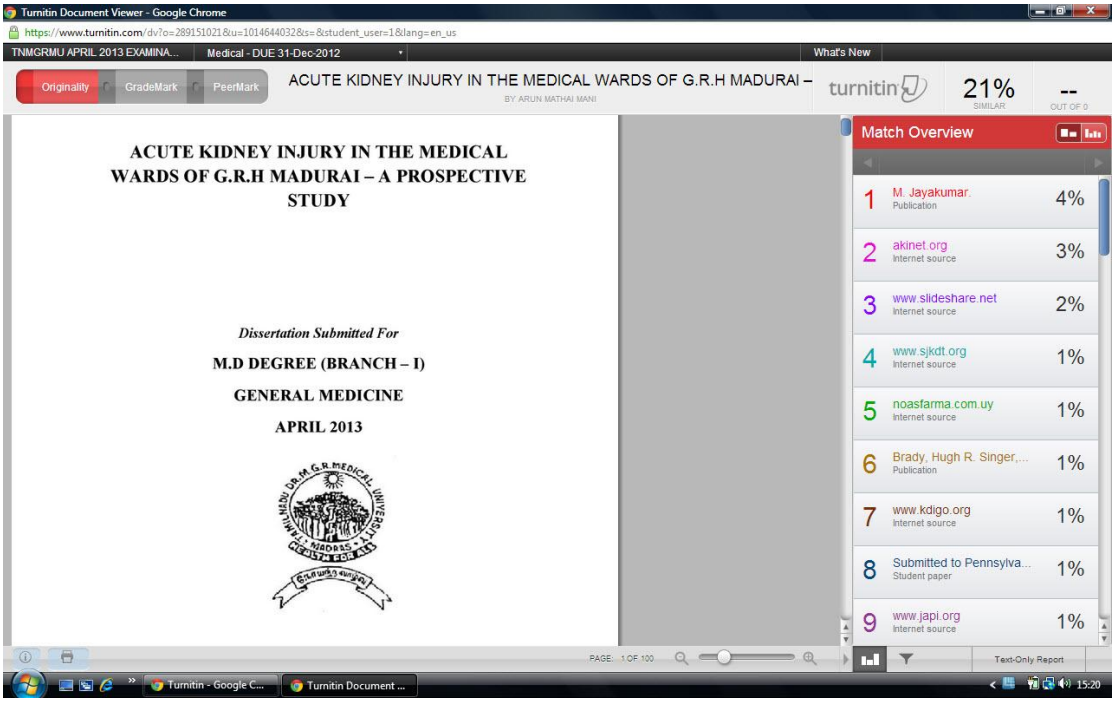
KEY TO MASTER CHART

ADD	ACUTE DIARRHEAL DISEASE
AGN	ACUTE GLOMERULONEPHRITIS
CAD	CORONARY ARTERY DISEASE
COPD	CHRONIC OBSTRUCTIVE PULMONARY DISEASE
CR	COMPLETE RECOVERY
CVA	CEREBROVASCULAR ACCIDENT
DM	DIABETES MELLITUS
HD	HEMODIALYSIS
HTN	HYPERTENSION
IHM	IN-HOSPITAL MORTALITY
PD	PERITONEAL DIALYSIS
PR	PARTIAL RECOVERY
TAFI	TROPICAL ACUTE FEBRILE ILLNESS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ACUTE KIDNEY INJURY IN THE MEDICAL WARDS OF G.R.H MADURAI – A PROSPECTIVE STUDY Dissertation Submitted For M.D DEGREE (BRANCH – I) GENERAL MEDICINE APRIL 2013 THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY CHENNAI 1 BONAFIDE CERTIFICATE This is to certify that the dissertation entitled “ACUTE KIDNEY INJURY IN THE MEDICAL WARDS OF G.R.H MADURAI – A PROSPECTIVE STUDY” submitted by Dr. ARUN MATHAI MANI to the Tamil Nadu Dr. M.G.R Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D DEGREE (Branch–I) GENERAL MEDICINE is a bonafide research work carried out by him under direct supervision & guidance. Prof. Dr. R Balajinathan MD Professor and Chief IV M.U...

MASTER CHART

sno	age	sex	durstay	diar	vomit	olig	breath	altsens	edema	neptox	uremsym	jaund	comor	hb	crHI
1	50	FEMALE	15	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	11	11.7
2	40	FEMALE	14	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8	5
3	55	MALE	15	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	DM	10	7.5
4	65	MALE	0	PRESENT	PRESENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	CAD	4	8.8
5	23	MALE	14	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	11	5.5
6	45	MALE	16	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	9	6
7	65	MALE	14	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	HTN	7	4.5
8	34	MALE	14	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	12	10
9	65	MALE	12	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	DM	10	9
10	35	MALE	13	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.5	7.6
11	64	FEMALE	16	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	DM	11	7
12	54	FEMALE	13	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	13.3	11
13	64	FEMALE	14	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8	7.5
14	15	MALE	5	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	2.8
15	13	MALE	6	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	3.3
16	60	MALE	7	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10	3
17	60	MALE	6	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	8.7	1.9
18	32	MALE	5	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11	5.5
19	58	MALE	8	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	3.9
20	55	MALE	6	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12.9	3.2
21	55	MALE	5	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	HTN	9.2	2.8
22	40	MALE	8	PRESENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.4	2.2
23	35	MALE	6	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	8	2.4
24	40	MALE	5	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	7.8	3.6
25	35	MALE	8	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.1	3
26	65	MALE	7	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.7	1.9
27	73	MALE	6	PRESENT	ABSENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	COPD	9.1	6
28	23	MALE	9	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10	2.9
29	14	MALE	6	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	7.8	2.1
30	45	MALE	4	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	3.8
31	43	MALE	6	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10	3.5
32	32	MALE	7	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	1.5
33	14	MALE	8	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	9.6	2.9
34	25	MALE	9	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	6.3	3.3
35	42	MALE	6	PRESENT	PRESENT	NON-OLIG	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	7	3.4
36	36	MALE	5	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.2	1.9

37	28	MALE	7	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	11	2.2
38	29	MALE	8	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8	3.1
39	39	MALE	9	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.2	4.8
40	49	MALE	8	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.8	1.6
41	62	MALE	6	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	CVA	10.8	3.3
42	35	FEMALE	6	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10	5.2
43	32	FEMALE	6	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	5.9	2
44	75	FEMALE	7	PRESENT	PRESENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	HTN	8.6	4.5
45	54	FEMALE	8	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.8	2.4
46	35	FEMALE	5	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.2	2.6
47	63	FEMALE	7	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12	3.8
48	25	FEMALE	5	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	DM	9.7	5.5
49	36	FEMALE	6	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	1.8
50	57	FEMALE	5	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.8	3.2
51	63	FEMALE	8	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10	3.5
52	26	FEMALE	6	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.8	3.4
53	29	FEMALE	9	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	7.9	1.5
54	36	FEMALE	5	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11.9	2.1
55	72	FEMALE	6	PRESENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	HTN	6.7	6.3
56	35	FEMALE	7	PRESENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	CAD	12.3	2.9
57	24	MALE	18	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.2	12.5
58	37	MALE	7	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.4	6.2
59	40	MALE	7	ABSENT	ABSENT	OLIGURIC	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	8.6	5.4
60	19	MALE	13	ABSENT	PRESENT	OLIGURIC	ABSENT	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	10	5.7
61	35	MALE	10	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12	10.7
62	38	MALE	19	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	9.9	9
63	31	MALE	13	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11.6	8.6
64	38	MALE	15	ABSENT	ABSENT	OLIGURIC	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12	2.5
65	67	MALE	5	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	DM	10	2.9
66	49	MALE	5	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	HTN	9.2	4
67	75	MALE	6	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	HTN	10.4	1.9
68	56	MALE	5	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.6	3.6
69	45	MALE	6	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.6	2.4
70	37	MALE	8	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11.8	2.2
71	28	MALE	6	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.8	1.6
72	16	MALE	8	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10	1.8
73	27	FEMALE	7	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	9.6	8.9
74	25	FEMALE	6	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.8	10

75	41	FEMALE	9	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12.5	6
76	36	FEMALE	7	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	10	4.3
77	37	FEMALE	6	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12	1.8
78	45	FEMALE	8	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	3.2
79	56	FEMALE	7	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11.2	1.7
80	37	FEMALE	6	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	8.9	2.3
81	45	MALE	0	ABSENT	PRESENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	DM	11.9	5.5
82	50	MALE	0	ABSENT	ABSENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.8	4.2
83	62	MALE	0	ABSENT	PRESENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	DM	10	3.9
84	70	MALE	0	ABSENT	ABSENT	OLIGURIC	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	DM	11	3.9
85	42	FEMALE	0	ABSENT	PRESENT	NON-OLIGU	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9	2.3
86	53	FEMALE	0	ABSENT	ABSENT	OLIGURIC	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.3	2.5
87	59	FEMALE	0	ABSENT	PRESENT	OLIGURIC	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	DM	9	2.9
88	24	MALE	14	ABSENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	12.7	2.5
89	45	MALE	10	ABSENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	9.2	5.5
90	70	MALE	10	ABSENT	PRESENT	OLIGURIC	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	CAD	12.8	5.1
91	56	FEMALE	12	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	DM	10.3	3.1
92	38	FEMALE	15	ABSENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11	1.9
93	53	MALE	13	ABSENT	ABSENT	OLIGURIC	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	8.4	9.8
94	19	MALE	0	ABSENT	PRESENT	OLIGURIC	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	12.4	13.6
95	40	FEMALE	10	ABSENT	PRESENT	OLIGURIC	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	9.5	4.8
96	32	MALE	0	ABSENT	PRESENT	NON-OLIGU	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.5	5.5
97	55	MALE	7	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	12	3.6
98	60	MALE	8	ABSENT	ABSENT	OLIGURIC	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	9.2	3.4
99	42	FEMALE	5	ABSENT	PRESENT	NON-OLIGU	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	10	2.4
100	47	FEMALE	8	ABSENT	PRESENT	OLIGURIC	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	12.4	4.5
101	19	MALE	21	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	11.6	12
102	25	MALE	7	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	7.2	3.2
103	29	MALE	9	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11.8	2.9
104	26	FEMALE	7	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.5	2.4
105	64	MALE	15	ABSENT	ABSENT	OLIGURIC	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	10.8	4.1
106	36	MALE	8	ABSENT	PRESENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	11.7	3.6
107	45	FEMALE	0	PRESENT	ABSENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	9.4	4.2
108	34	FEMALE	0	ABSENT	ABSENT	OLIGURIC	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	13.6	4.5
109	23	FEMALE	22	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	11	1.9
110	29	FEMALE	18	ABSENT	ABSENT	NON-OLIGU	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	10.8	2.2
111	35	FEMALE	18	ABSENT	ABSENT	OLIGURIC	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	9.2	9.2
112	35	MALE	26	ABSENT	ABSENT	OLIGURIC	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	10.2	16.2

urea	aki	rrt	rrttype	rrtfreq	rrtind	outcom	findiag	satgeFI
223	AT	YES	HD	2	SERUM CREATININE >4mg/dl	CR	ADD	AKIN 3
112	AFTER	YES	PD	1	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
131	AT	YES	PD	1	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
293	AFTER	YES	HD	2	SYMPTOMATIC UREMIA	IHM	ADD	AKIN 3
112	AT	YES	HD	2	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
102	AT	YES	HD	2	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
166	AT	YES	HD	3	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
148	AT	YES	HD	2	SERUM CREATININE >4mg/dl	CR	ADD	AKIN 3
131	AT	YES	HD	2	SERUM CREATININE >4mg/dl	CR	ADD	AKIN 3
154	AFTER	YES	PD	1	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
114	AT	YES	HD	2	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
106	AT	YES	HD	2	SERUM CREATININE >4mg/dl	CR	ADD	AKIN 3
120	AFTER	YES	PD	1	SYMPTOMATIC UREMIA	CR	ADD	AKIN 3
115	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
47	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
56	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
70	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
176	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
90	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
94	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
115	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
55	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
110	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
56	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
78	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
76	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
88	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
70	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
67	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
68	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
67	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
52	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
45	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
67	AT	NO	NA	NA	NA	CR	ADD	AKIN 2
82	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
56	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1

81	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
62	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
78	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
62	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
55	AT	NO	NA	NA	NA	CR	ADD	AKIN 2
75	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
61	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
192	AT	NO	NA	NA	NA	CR	ADD	AKIN 3
101	AT	NO	NA	NA	NA	CR	ADD	AKIN 2
60	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
80	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
58	AT	NO	NA	NA	NA	CR	ADD	AKIN 3
108	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
54	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
82	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
67	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 3
68	AT	NO	NA	NA	NA	CR	ADD	AKIN 1
84	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 1
45	AT	NO	NA	NA	NA	CR	ADD	AKIN 3
86	AFTER	NO	NA	NA	NA	CR	ADD	AKIN 2
56	AT	YES	HD	6	SERUM CREATININE >4mg/dl	CR	Snake BIte	AKIN 3
48	AFTER	YES	HD	3	SYMPTOMATIC UREMIA	CR	Snake BIte	AKIN 3
56	AT	YES	PD	1	SYMPTOMATIC UREMIA	CR	Snake BIte	AKIN 3
50	AFTER	YES	HD	3	SYMPTOMATIC UREMIA	CR	Snake BIte	AKIN 3
164	AFTER	YES	HD	8	SERUM CREATININE >4mg/dl	CR	Snake BIte	AKIN 3
150	AFTER	YES	HD	4	SYMPTOMATIC UREMIA	CR	Snake BIte	AKIN 3
163	AT	YES	HD	5	SERUM CREATININE >4mg/dl	CR	Snake BIte	AKIN 3
140	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
66	AT	NO	NA	NA	NA	CR	Snake BIte	AKIN 2
78	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 3
69	AT	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
161	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 3
50	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
67	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
56	AT	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
86	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
150	AT	YES	HD	2	SERUM CREATININE >4mg/dl	CR	Snake BIte	AKIN 3
120	AT	YES	HD	3	SERUM CREATININE >4mg/dl	CR	Snake BIte	AKIN 3

140	AFTER	YES	HD	2	SYMPTOMATIC UREMIA	CR	Snake BIte	AKIN 3
163	AT	YES	PD	1	SYMPTOMATIC UREMIA	CR	Snake BIte	AKIN 3
68	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
84	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 3
86	AT	NO	NA	NA	NA	CR	Snake BIte	AKIN 1
72	AFTER	NO	NA	NA	NA	CR	Snake BIte	AKIN 2
108	AT	YES	HD	1	SYMPTOMATIC UREMIA	IHM	Sepsis	AKIN 3
114	AT	YES	HD	1	SYMPTOMATIC UREMIA	IHM	Sepsis	AKIN 3
98	AT	YES	PD	1	SYMPTOMATIC UREMIA	IHM	Sepsis	AKIN 3
78	AT	NO	NA	NA	NA	IHM	Sepsis	AKIN 3
54	AFTER	NO	NA	NA	NA	IHM	Sepsis	AKIN 2
45	AFTER	NO	NA	NA	NA	IHM	Sepsis	AKIN 2
84	AFTER	NO	NA	NA	NA	IHM	Sepsis	AKIN 3
88	AT	NO	NA	NA	NA	CR	Sepsis	AKIN 1
61	AT	YES	HD	2	SYMPTOMATIC UREMIA	CR	Sepsis	AKIN 3
126	AT	YES	PD	1	SYMPTOMATIC UREMIA	CR	Sepsis	AKIN 3
48	AT	NO	NA	NA	NA	CR	Sepsis	AKIN 2
82	AFTER	NO	NA	NA	NA	CR	Sepsis	AKIN 1
296	AT	YES	HD	5	SERUM CREATININE >4mg/dl	CR	TAFI	AKIN 3
154	AFTER	NO	NA	NA	NA	IHM	TAFI	AKIN 3
134	AFTER	YES	HD	2	SYMPTOMATIC UREMIA	CR	TAFI	AKIN 3
58	AFTER	NO	NA	NA	NA	IHM	TAFI	AKIN 3
83	AT	NO	NA	NA	NA	CR	TAFI	AKIN 3
73	AFTER	NO	NA	NA	NA	CR	TAFI	AKIN 2
96	AFTER	NO	NA	NA	NA	CR	TAFI	AKIN 1
68	AT	NO	NA	NA	NA	CR	TAFI	AKIN 3
199	AFTER	YES	HD	13	SYMPTOMATIC UREMIA	PR	AGN	AKIN 3
98	AT	NO	NA	NA	NA	CR	AGN	AKIN 2
80	AT	NO	NA	NA	NA	CR	AGN	AKIN 1
89	AT	NO	NA	NA	NA	CR	AGN	AKIN 1
68	AT	NO	NA	NA	NA	CR	NSAID Induced	AKIN 3
135	AT	NO	NA	NA	NA	CR	Copper Sulfate Poisoning	AKIN 2
67	AT	NO	NA	NA	NA	IHM	Copper Sulfate Poisoning	AKIN 3
87	AFTER	YES	HD	1	SYMPTOMATIC UREMIA	IHM	Supervasmol Poisoning	AKIN 3
66	AFTER	NO	NA	NA	NA	CR	Supervasmol Poisoning	AKIN 1
69	AFTER	NO	NA	NA	NA	CR	Supervasmol Poisoning	AKIN 1
108	AT	YES	HD	5	SYMPTOMATIC UREMIA	CR	Pigment Nephropathy	AKIN 3
240	AFTER	YES	HD	11	SERUM CREATININE >4mg/dl	PR	Pigment Nephropathy	AKIN 3